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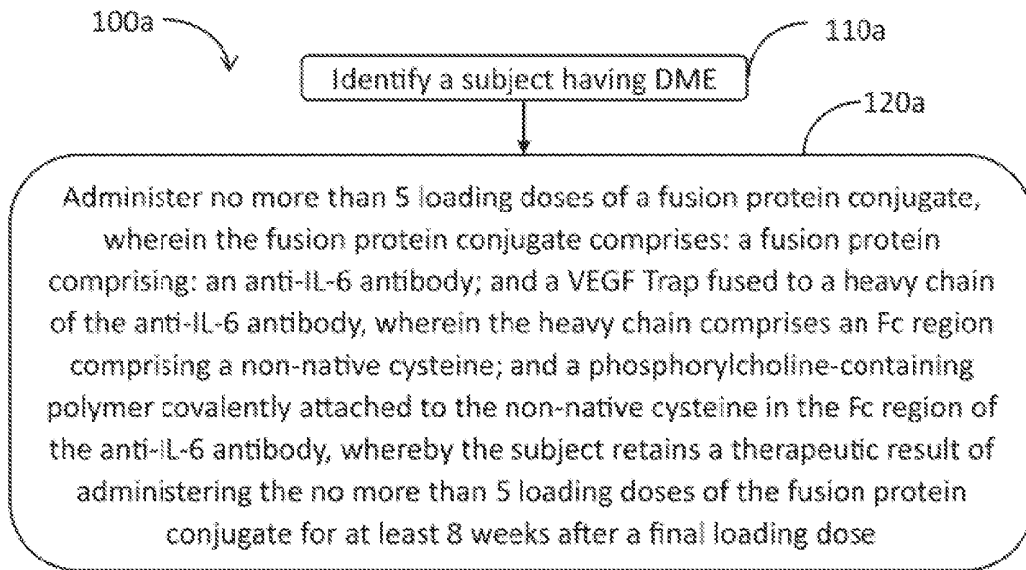


FIG. 1A

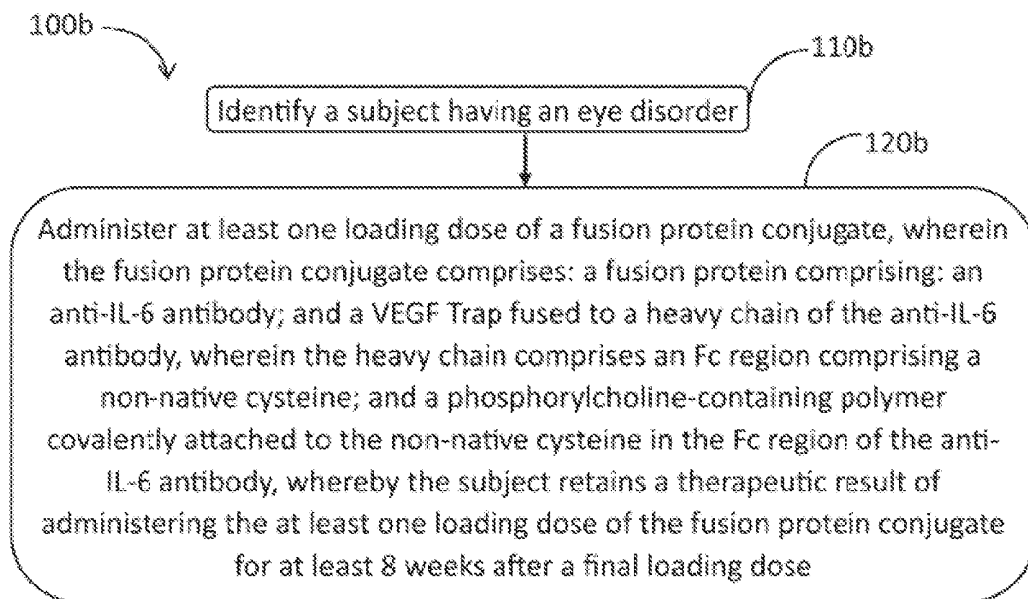


FIG. 1B

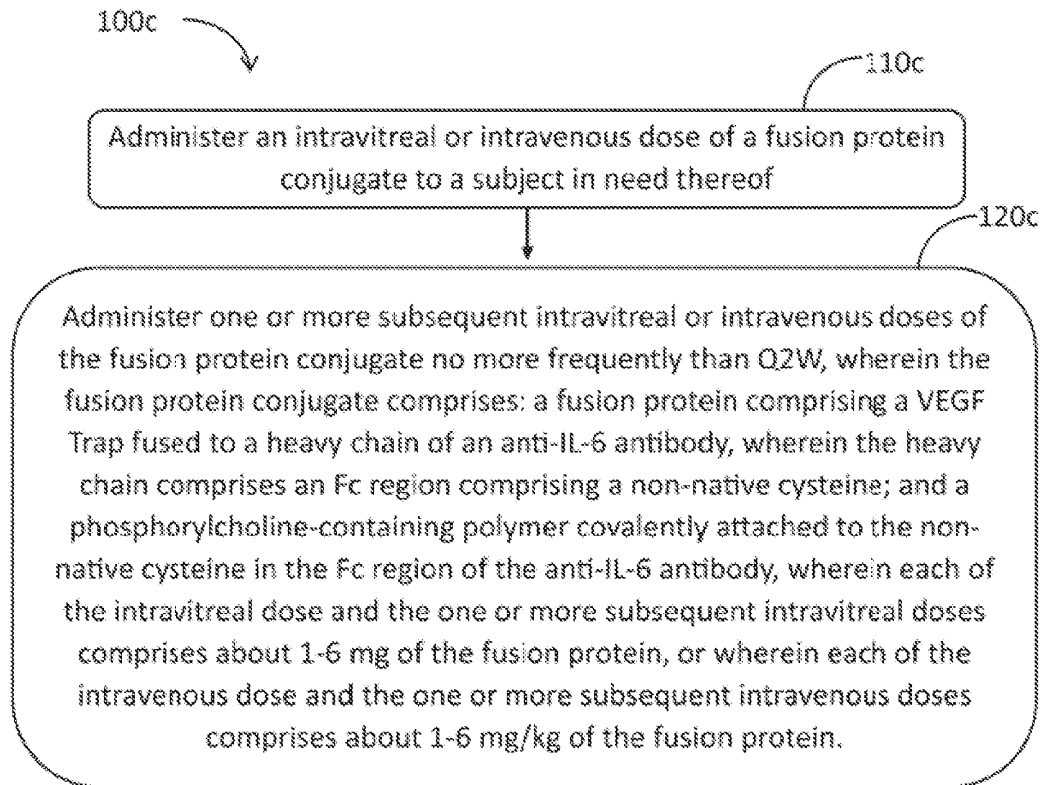
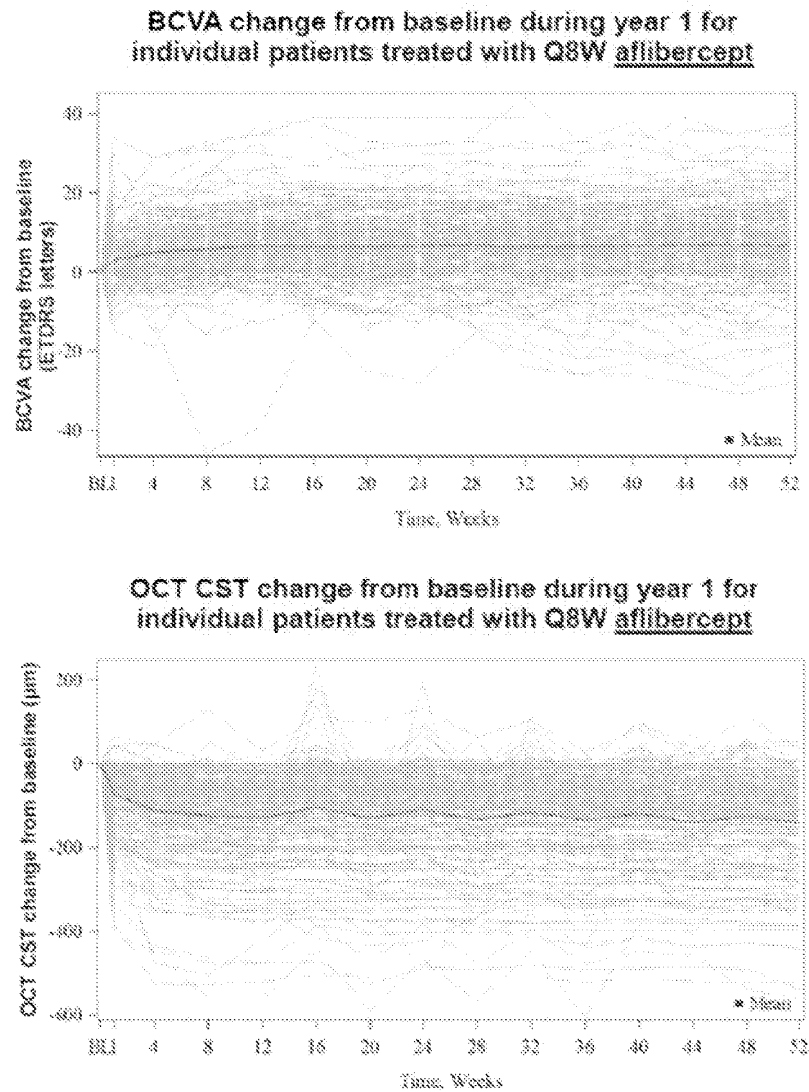


FIG. 1C



Aflibercept-treated subjects completing Year 1 of Phase 2b/3 study of tarcocimab tedromer in wet AMD, NCT04049266.

BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; OCT, optical coherence tomography; CST, central subfield thickness

FIG. 2

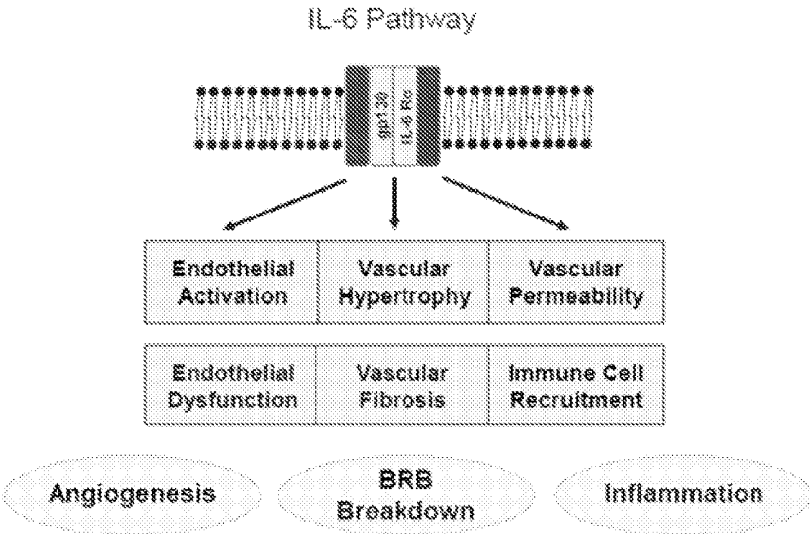


FIG. 3A

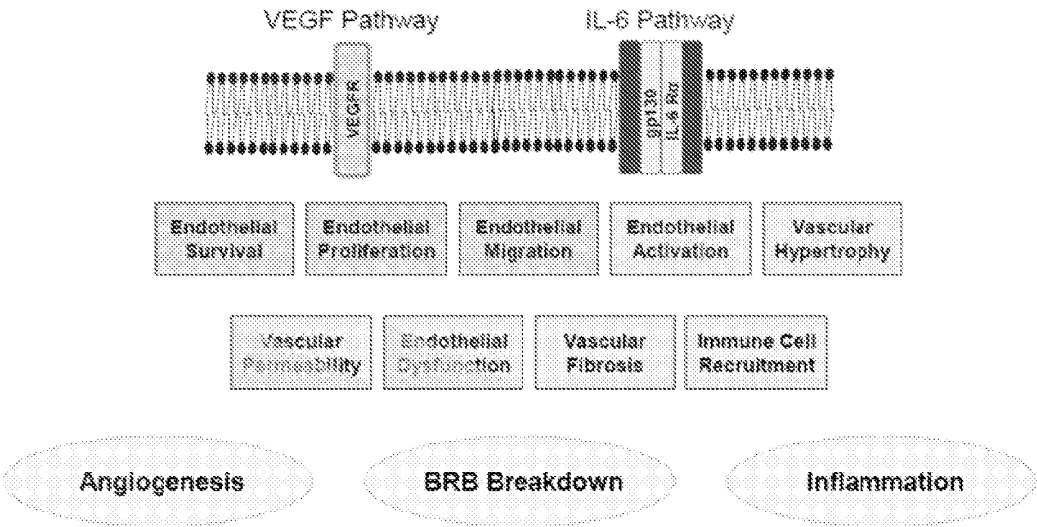


FIG. 3B

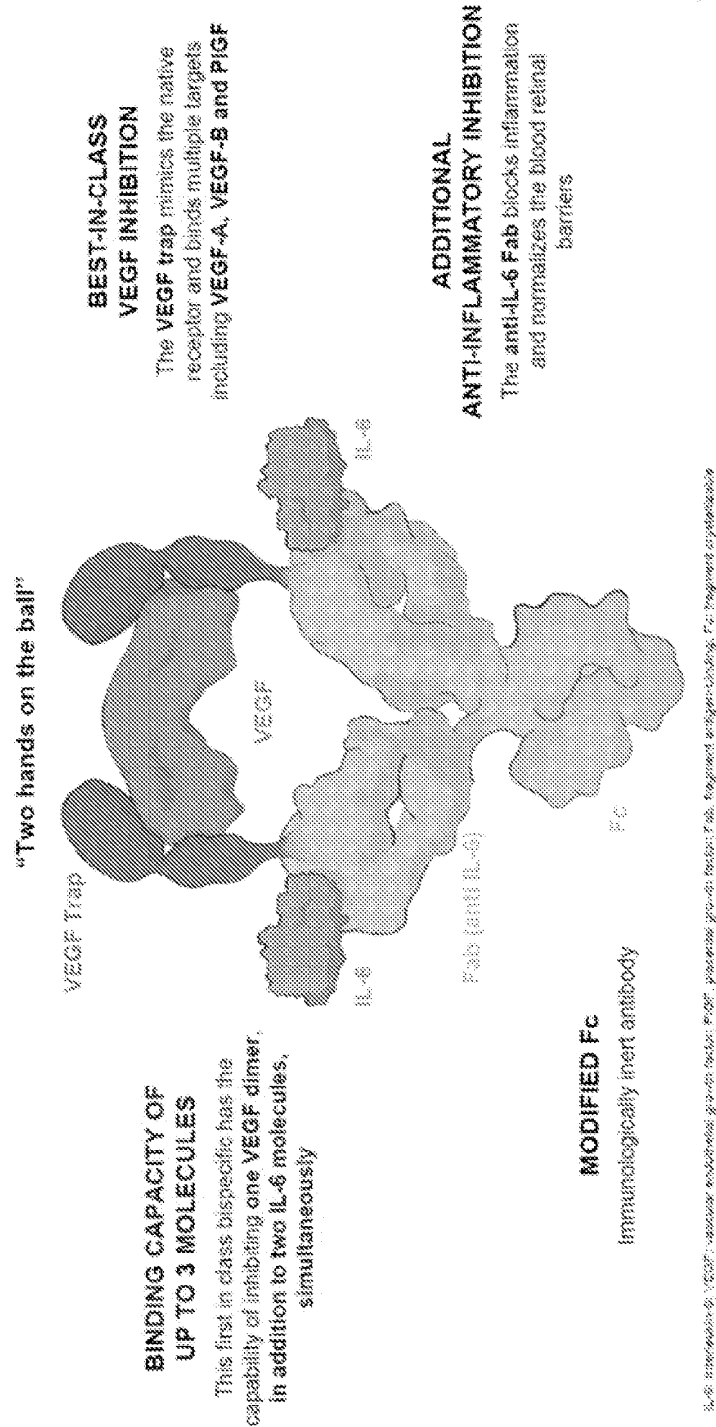


FIG. 4

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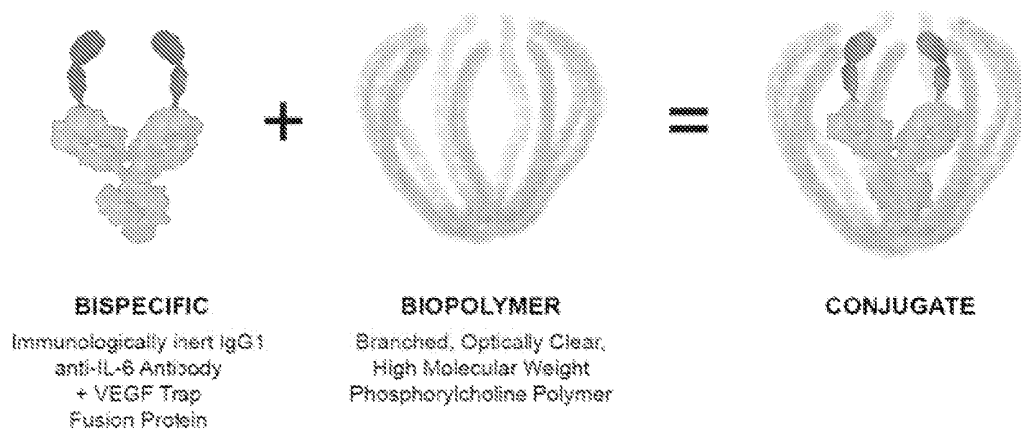


FIG. 5

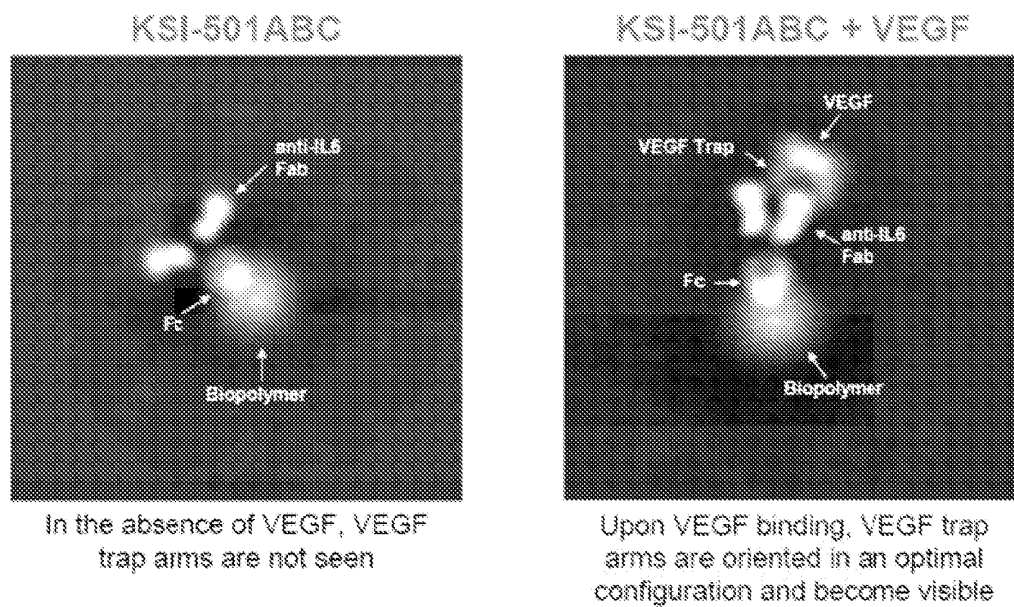


FIG. 6

Key disease drivers in retinal diseases	Aflibercept			Vamkibart (anti-IL-6 mAb)		KSI-501*	
	✓	✓	✓	✓	✓	✓	✓
	✓	✓	✓	✗	✗	✓	✓
	✓	✓	✓	✓	✓	✓	✓
	✓	✓	✓	✗	✗	✓	✓
Preclinical potency							
Binding affinity to VEGF-A†	0.49 pM			N/A		1.02 pM	
Inhibition of VEGF-A binding to VEGF-R**	IC ₅₀ =129.6 pM			N/A		IC ₅₀ =163.7 pM	
Inhibition of IL-6 cis signaling	N/A			IC ₅₀ = 41 pM		IC ₅₀ = 66 pM	
Inhibition of IL-6 trans signaling	N/A			IC ₅₀ = 1.0 nM		IC ₅₀ = 2.1 nM	
Target inhibition	VEGF-A, VEGF-B and PlGF			IL-6		VEGF-A, VEGF-B, PlGF and IL-6	
	✓			✓		✓	

retinal macular disease. *VEGF-A binding affinity determined by K₁₅₅ from Kinetic Exclusion assay for Vamkibart and KSI-501 and determined by Biacore from Biacore assay for aflibercept. **IC₅₀ determined by K₁₅₅ from VEGF inhibition assay. †IC₅₀ values for KSI-501 are shown. ‡IC₅₀ values for VEGF-A binding affinity, for which values for KSI-501 are shown.

FIG. 7

- Inner blood-retinal barrier: leakage from vascular endothelium disruption leads to macular edema and hemorrhage¹
- Outer blood-retinal barrier: RPE integrity prevents choroidal vascularization from invading the retina²

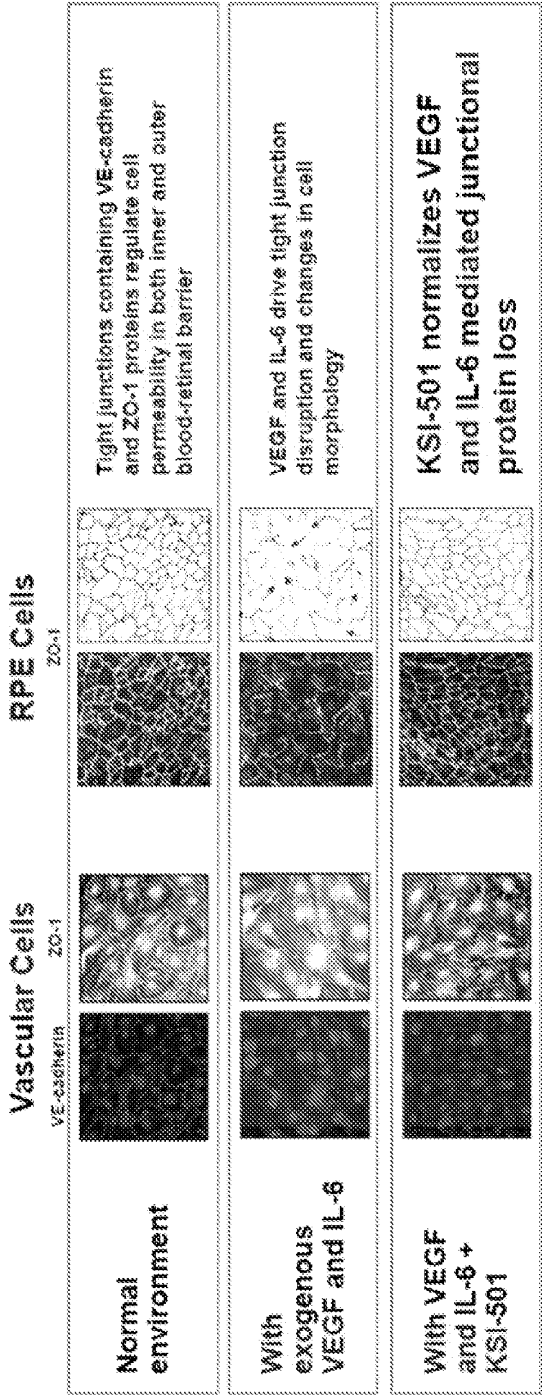


FIG. 8

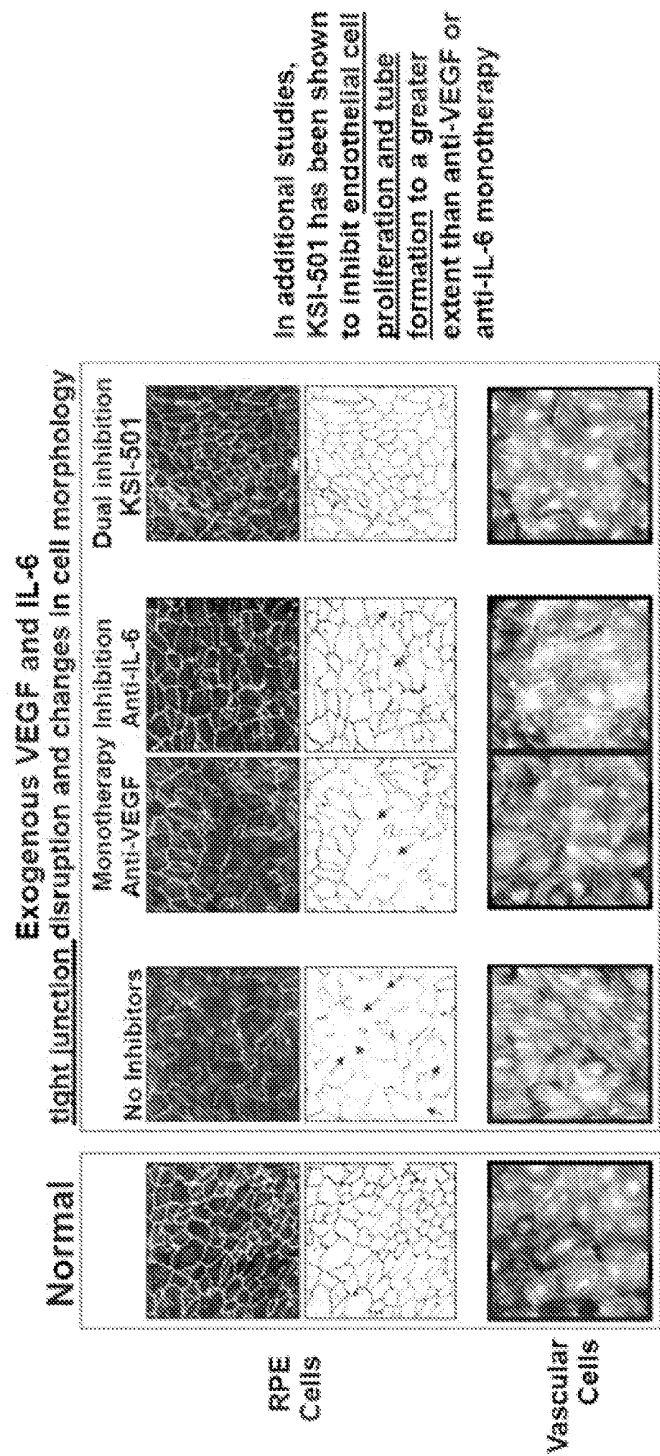


FIG. 9

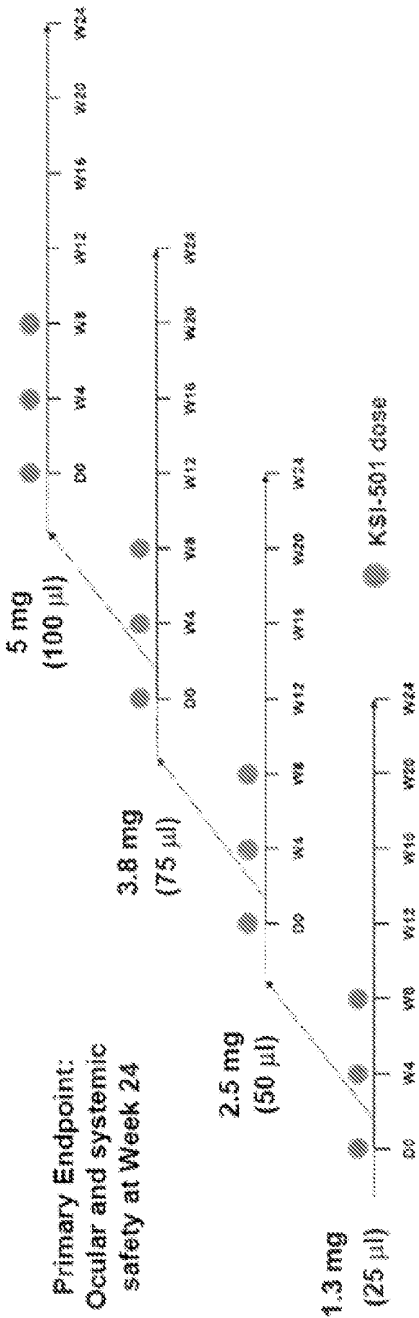


FIG. 10

	KSI-501 ABC n=16
Age, years, mean (SD)	67.3 (7.4)
Female, n (%)	6 (37.5)
Hemoglobin A1c, % (SD)	7.2 (1.2)
Diabetes Type 2, n (%)	14 (87.5%)
DME disease duration, months (SD)	38.3 (40.4)
BCVA, ETDRS Letters, mean (SD)	61.7 (9.2)
Snellen equivalent	~20/63
OCT Central Subfield Thickness (CST), μm , mean (SD)	446.0 (109.9)
Lens Status, n (%)	
Phakic	11 (68.8)
Pseudophakic	5 (31.3)
Intraocular Pressure, mmHg, mean (SD)	15.3 (2.9)

FIG. 11

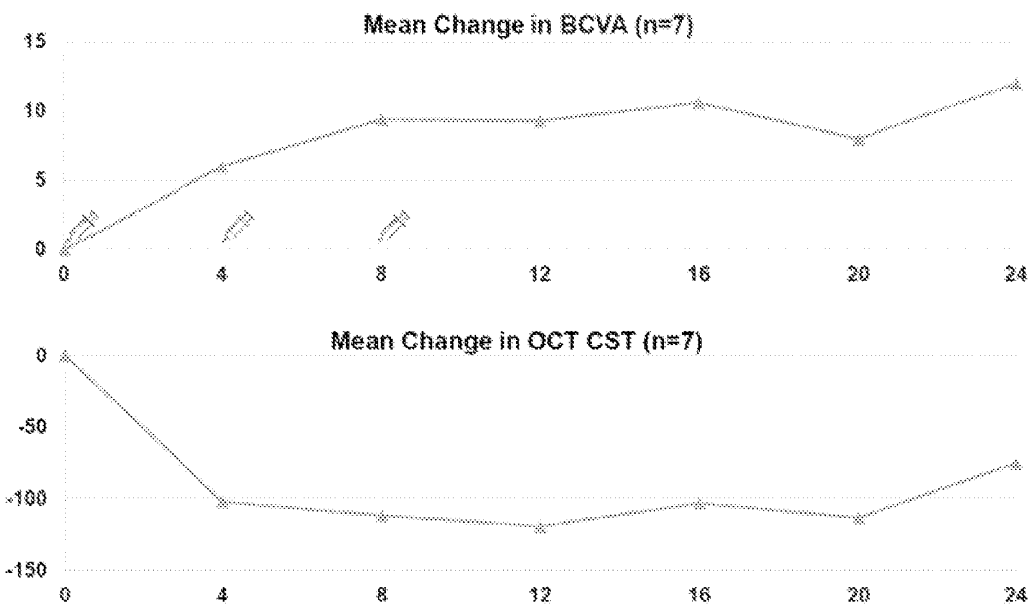


FIG. 12A

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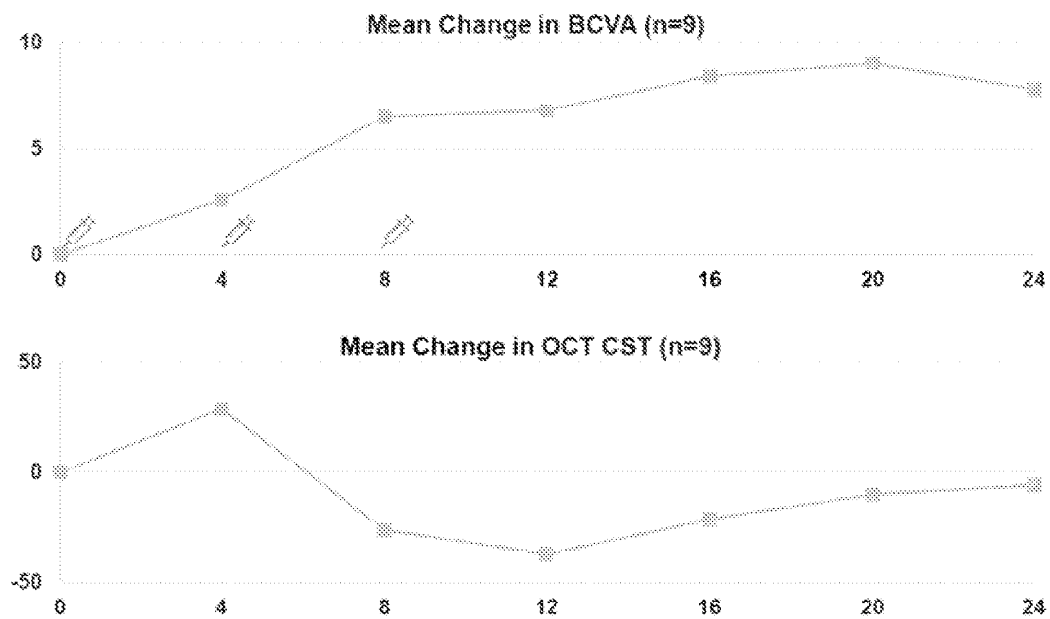


FIG. 12B

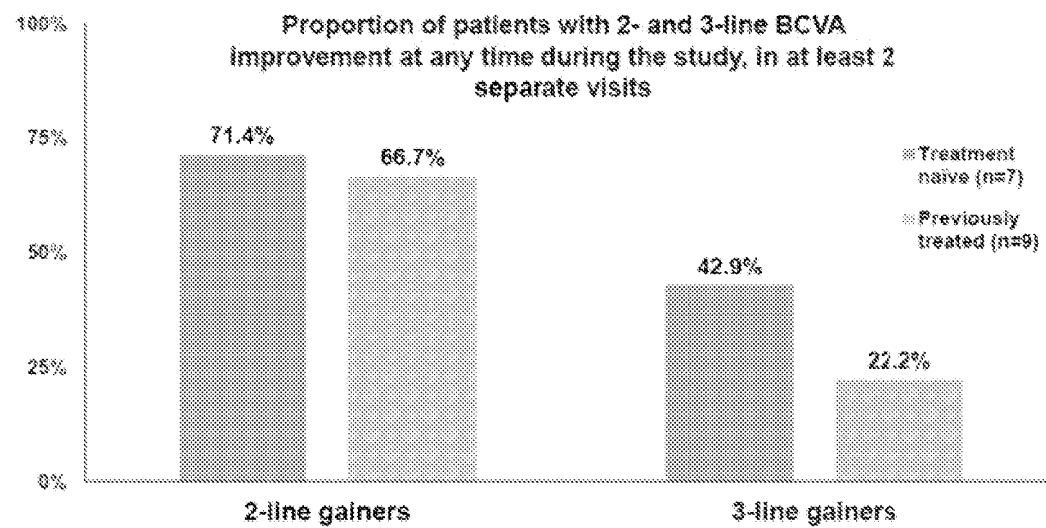


FIG. 12C

VPPGEDSKDVAAPHRQPLTSSERIDKQIRYILDGISAALRKETCNKSNMCESSEKALAEENNINLPKMAEKDG
CFQSGFNEETCLVKITGLLEFEVYLEYIQNRFESEEQARAVQMSTKVLIQFLQKKAKNLDAITTPDPTTN
ASLLTKLQAQNQWLQDMTHILRSFKEFLQSSLRALRQM (SEQ ID NO: 1)

FIG. 13

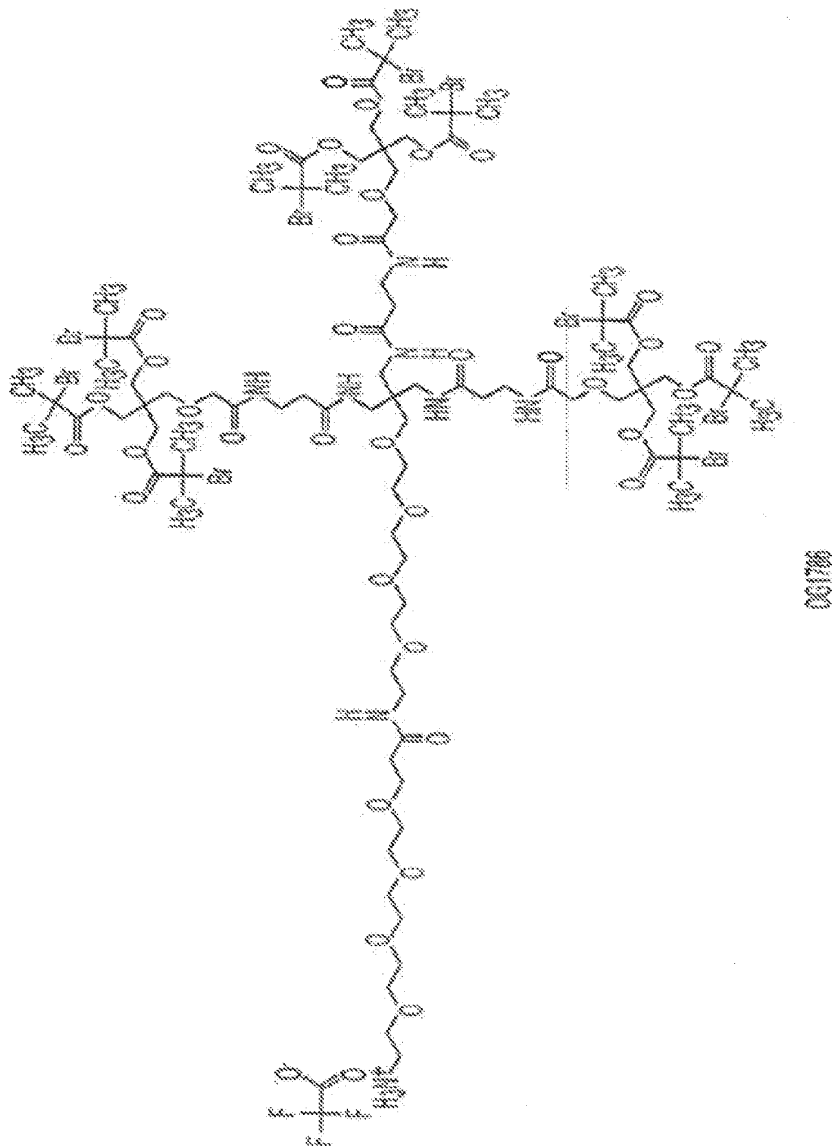
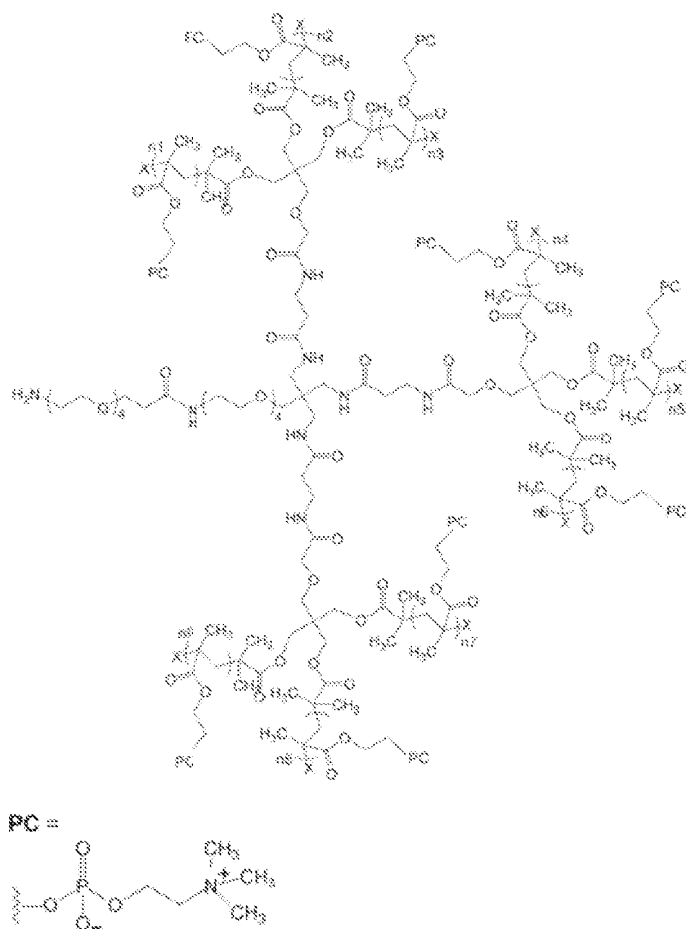


FIG. 14A

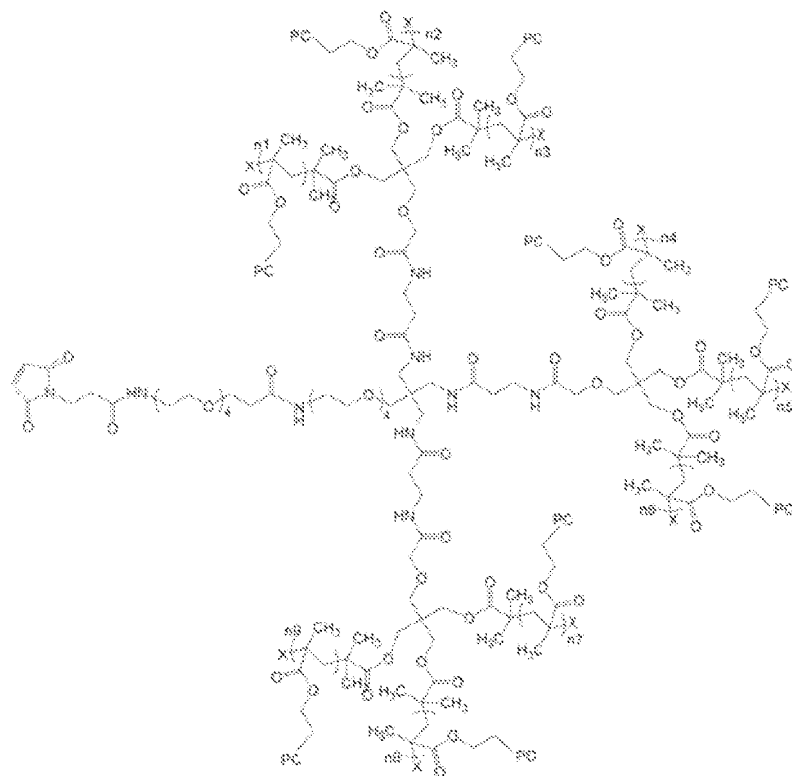
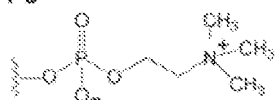
OG1801



—X is: a) —OR where R is H, methyl, ethyl, propyl, isopropyl; b) —H; or c) any halogen, including —Br, —Cl, or —I; d) —SCN; or e) —NCS, and n1, n2, n3, n4, n5, n6, n7, n8 and n9 are the same or different such that the sum of n1, n2, n3, n4, n5, n6, n7, n8 and n9 is 2500 plus or minus 15%.

FIG. 14B

OG1802

**Definitions:****PC =**

--X is: a) --OR where R is H, methyl, ethyl, propyl, isopropyl; b) --H; or c) any halogen, including --Br, --Cl, or --I; d) --SCN; or e) --NCS, and n1, n2, n3, n4, n5, n6, n7, n8 and n9 are the same or different such that the sum of n1, n2, n3, n4, n5, n6, n7, n8 and n9 is 2500 plus or minus 15%.

FIG. 14C

Heavy Chain	EVQLVESGGGLVQPGGSLRLSCAAS[GFTSPFAIS]WYRQAPGKGLEW[VAKISPGGSWTYYSDIVTD] RFTFSLDTSKSTAYLQMNSLRAEDTAVYYC[ARQLWGYALDV]WGQGILVTVSS (SEQ ID NO: 2)
Light Chain	DIQLTQSPSSLASVGDRTTTC[SASISVSILY]WYQQKPGKAPK[LLIYDDSSLAS]GVPSRFSGSGGTD FILTISSLQPEDFATYYC[QQWSGYPYT]FGGGTKVEIK (SEQ ID NO: 3)

FIG. 15

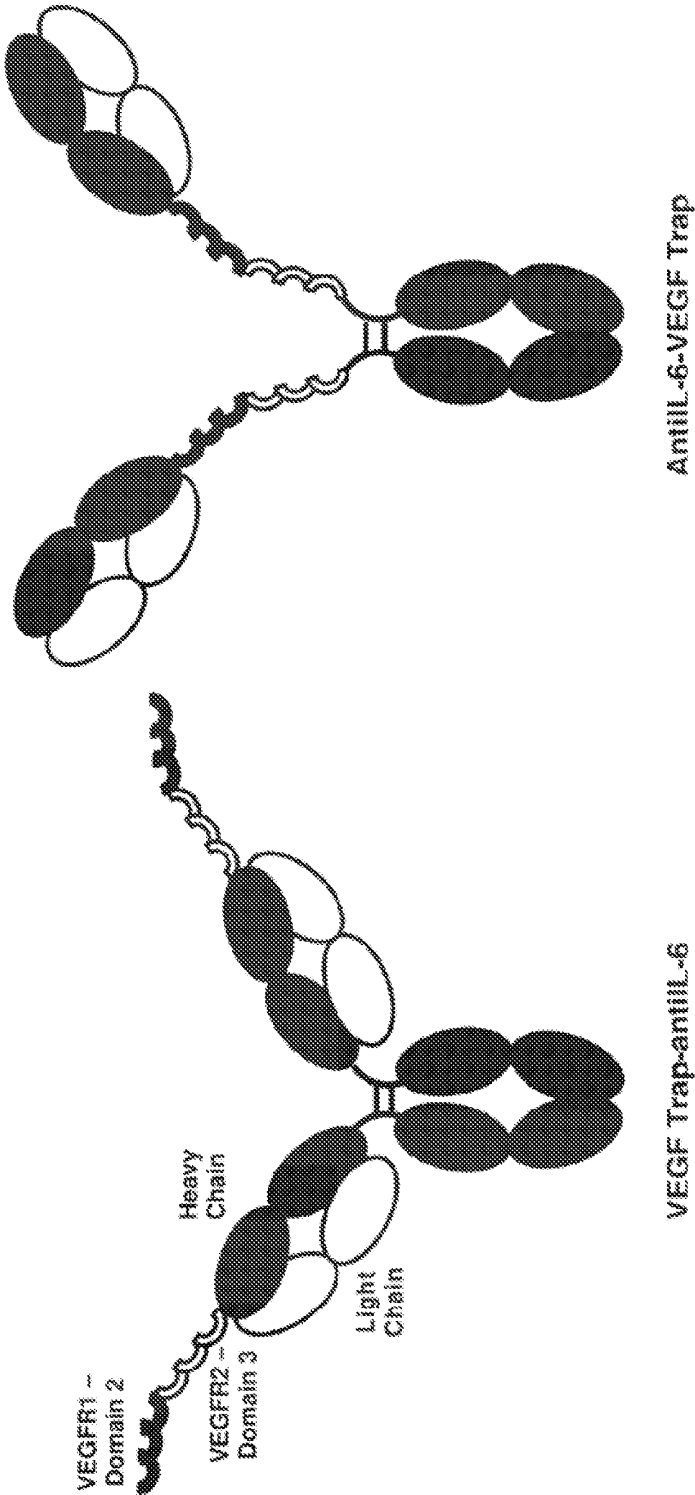


FIG. 16



FIG. 17

> VEGF_trap_Variant_1
(SEQ ID NO: 4)
SDTGRPFVEMYSSEPEHNAITEGRELVPICRVTSPTNIVTLKKFPLDTLIPDGKRHWDSKKGHHSNATYKEIGLLTCEATVN
GHLVKTNVLEHQINTHDVLSPSHGIELSVGEKLVNCTARTIELNVGIDFNWEYPSKKHQKKLVNRDLKTQSGSEM
KKFLSTLTIDGVTRSDQGLYTCAASSGLMTKKNSTFVRVHEK

> VEGF_trap_Variant_2
(SEQ ID NO: 5)
SDTGRPFVEMYSSEPEHNAITEGRELVPICRVTSPTNIVTLKKFPLDTLIPDGKRHWDSKKGHHSNATYKEIGLLTCEATVN
GHLVKTNVLEHQINTHDVLSPSHGIELSVGEKLVNCTARTIELNVGIDFNWEYPSKKHQKKLVNRDLKTQSGSEM
KKFLSTLTIDGVTRSDQGLYTCAASSGLMTKKNSTFVRVHEK

> VEGF_trap_Variant_3
(SEQ ID NO: 6)
SDTGRPFVEMYSSEPEHNAITEGRELVPICRVTSPTNIVTLKKFPLDTLIPDGKRHWDSKKGHHSNATYKEIGLLTCEATVN
GHLVKTNVLEHQINTHDVLSPSHGIELSVGEKLVNCTARTIELNVGIDFNWEYPSKKHQKKLVNRDLKTQSGSEM
KKFLSTLTIDGVTRSDQGLYTCAASSGLMTKKNSTFVRVHEK

FIG. 18

ID	Sequence
VI	EVQLVESGGGLVQPGGSLRLSCAASGFTSPFAMHWVROAPGKGLEWVAKISFGGSWLYISDIYIDRFIF SLDTSKSTAYLQMSLRAEDTAVYYCARQAWGVYALDIWGQGHLVTVSS
VII	EVQLVESGGGLVQPGGSLRLSCAASGFTSPFAMHWVROAPGKGLEWVAKISFGGSWLYISDIYIDRFIF SLDTSKSTAYLQMSLRAEDTAVYYCARQSWGVYALDIWGQGHLVTVSS
VIII	EVQLVESGGGLVQPGGSLRLSCAASGFTSPFAMHWVROAPGKGLEWVAKISFGGSWLYISDIYIDRFIF SLDTSKSTAYLQMSLRAEDTAVYYCARQGVYALDIWGQGHLVTVSS
IX	EVQLVESGGGLVQPGGSLRLSCAASGFTSPFAMHWVROAPGKGLEWVAKISFGGSWLYISDIYIDRFIF SLDTSKSTAYLQMSLRAEDTAVYYCARQGVYALDIWGQGHLVTVSS
X	EVQLVESGGGLVQPGGSLRLSCAASGFTSPFAMHWVROAPGKGLEWVAKISFGGSWLYISDIYIDRFIF SLDTSKSTAYLQMSLRAEDTAVYYCARQGVYALDIWGQGHLVTVSS
XI	EVQLVESGGGLVQPGGSLRLSCAASGFTSPFAMHWVROAPGKGLEWVAKISFGGSWLYISDIYIDRFIF SLDTSKSTAYLQMSLRAEDTAVYYCARQGVYALDIWGQGHLVTVSS
XII	EVQLVESGGGLVQPGGSLRLSCAASGFTSPFAMHWVROAPGKGLEWVAKISFGGSWLYISDIYIDRFIF SLDTSKSTAYLQMSLRAEDTAVYYCARQGVYALDIWGQGHLVTVSS
XIII	EVQLVESGGGLVQPGGSLRLSCAASGFTSPFAMHWVROAPGKGLEWVAKISFGGSWLYISDIYIDRFIF SLDTSKSTAYLQMSLRAEDTAVYYCARQGVYALDIWGQGHLVTVSS

FIG. 19

ID	VEGF Trap Sequence
1A	SDTGRFFVENYSEIPEIHHMTEGRELVIPCRVTSFNITVTLKKFFLDLIPDGKRHWDSRKGFHSNATYKEIGL LTCEATVNGHL YKTNVLIHQQTNIHIDVVLSPSHGIELSVGEKLVLNCTARTELNVGIDFNWEYPSSKHQHK KKLVNRDLKTQSGSEMKKFSTLTIDGVTRSDQGLYTCAASSGLMTKKNSTFVRVHEK
1B	SDTGRFFVENYSEIPEIHHMTEGRELVIPCRVTSFNITVTLKKFFLDLIPDGKRHWDSRKGFHSNATYKEIGL LTCEATVNGHL YKTNVLIHQQTNIHIDVVLSPSHGIELSVGEKLVLNCTARTELNVGIDFNWEYPSSKHQHK KKLVNRDLKTQSGSEMKKFSTLTIDGVTRSDQGLYTCAASSGLMTKKNSTFVRVHEK
1C	SDTGRFFVENYSEIPEIHHMTEGRELVIPCRVTSFNITVTLKKFFLDLIPDGKRHWDSRKGFHSNATYKEIGL LTCEATVNGHL YKTNVLIHQQTNIHIDVVLSPSHGIELSVGEKLVLNCTARTELNVGIDFNWEYPSSKHQHK KKLVNRDLKTQSGSEMKKFSTLTIDGVTRSDQGLYTCAASSGLMTKKNSTFVRVHEK
1D	SDTGRFFVENYSEIPEIHHMTEGRELVIPCRVTSFNITVTLKKFFLDLIPDGKRHWDSRKGFHSNATYKEIGL LTCEATVNGHL YKTNVLIHQQTNIHIDVVLSPSHGIELSVGEKLVLNCTARTELNVGIDFNWEYPSSKHQHK KKLVNRDLKTQSGSEMKKFSTLTIDGVTRSDQGLYTCAASSGLMTKKNSTFVRVHEK

(SEQ ID NO: 14)

(SEQ ID NO: 15)

(SEQ ID NO: 16)

(SEQ ID NO: 17)

FIG. 20

(SEQ ID NO: 18)

ID	Linker Sequence
2A	GGGGGGGGGG

FIG. 21

ID	Heavy chain Sequence
3A	EVQLVESGGGLVQPGGSLRLSCAASGFTESFEAMHWVRQAPGKGLEWVAKISPGGGSW ¹ TYSDTVTD ² DRFTF SLDTSKSTAYLQMNSLRAEDTAVYYCARQAWGYYALDIWGQGT ³ LVTVSSASTKGPSVF ⁴ PLAPSSKSTSGG TAALGCLYKDYFPEPVT ⁵ VSWSNGALTSGVHTT ⁶ PAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVN ⁷ NHKPSNTK VDKKVEPKSCDKTHTCTPPCPAPEAAGAPSVFL ⁸ PPKPKDITLMISRTPEVTCVVDVSHED ⁹ EVKFNWYVDG VEVHNAKTKPREEQYNSTYRVVSVLT ¹⁰ VLHQDWLNQKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL PPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNCPENNYK ¹¹ TPPVLDSDGSFFLYSKLTVDKSRWQQGN VFSCSYMIHEALHNHYTQKSLS ¹² CSPGK (SEQ ID NO: 19)
3B	EVQLVESGGGLVQPGGSLRLSCAASGFTESFEAMHWVRQAPGKGLEWVAKISPGGGSW ¹ TYSDTVTD ² DRFTF SLDTSKSTAYLQMNSLRAEDTAVYYCARQAWGYYALDIWGQGT ³ LVTVSSASTKGPSVF ⁴ PLAPSSKSTSGG TAALGCLYKDYFPEPVT ⁵ VSWSNGALTSGVHTT ⁶ PAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVN ⁷ NHKPSNTK VDKKVEPKSCDKTHTCTPPCPAPEAAGAPSVFL ⁸ PPKPKDITLMISRTPEVTCVVDVSHED ⁹ EVKFNWYVDG VEVHNAKTKPREEQYNSTYRVVSVLT ¹⁰ VLHQDWLNQKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL PPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNCPENNYK ¹¹ TPPVLDSDGSFFLYSKLTVDKSRWQQGN VFSCSYMIHEALHNHYTQKSLS ¹² CSPGK (SEQ ID NO: 20)
3C	EVQLVESGGGLVQPGGSLRLSCAASGFTESFEAMHWVRQAPGKGLEWVAKISPGGGSW ¹ TYSDTVTD ² DRFTF SLDTSKSTAYLQMNSLRAEDTAVYYCARQAWGYYALDIWGQGT ³ LVTVSSASTKGPSVF ⁴ PLAPSSKSTSGG TAALGCLYKDYFPEPVT ⁵ VSWSNGALTSGVHTT ⁶ PAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVN ⁷ NHKPSNTK VDKKVEPKSCDKTHTCTPPCPAPEAAGAPSVFL ⁸ PPKPKDITLMISRTPEVTCVVDVSHED ⁹ EVKFNWYVDG VEVHNAKTKPREEQYNSTYRVVSVLT ¹⁰ VLHQDWLNQKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL PPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNCPENNYK ¹¹ TPPVLDSDGSFFLYSKLTVDKSRWQQGN VFSCSYMIHEALHNHYTQKSLS ¹² CSPGK (SEQ ID NO: 21)
3D	EVQLVESGGGLVQPGGSLRLSCAASGFTESFEAMHWVRQAPGKGLEWVAKISPGGGSW ¹ TYSDTVTD ² DRFTF SLDTSKSTAYLQMNSLRAEDTAVYYCARQAWGYYALDIWGQGT ³ LVTVSSASTKGPSVF ⁴ PLAPSSKSTSGG TAALGCLYKDYFPEPVT ⁵ VSWSNGALTSGVHTT ⁶ PAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVN ⁷ NHKPSNTK VDKKVEPKSCDKTHTCTPPCPAPEAAGAPSVFL ⁸ PPKPKDITLMISRTPEVTCVVDVSHED ⁹ EVKFNWYVDG VEVHNAKTKPREEQYNSTYRVVSVLT ¹⁰ VLHQDWLNQKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL PPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNCPENNYK ¹¹ TPPVLDSDGSFFLYSKLTVDKSRWQQGN VFSCSYMIHEALHNHYTQKSLS ¹² CSPGK (SEQ ID NO: 22)
3E	EVQLVESGGGLVQPGGSLRLSCAASGFTESFEAMHWVRQAPGKGLEWVAKISPGGGSW ¹ TYSDTVTD ² DRFTF SLDTSKSTAYLQMNSLRAEDTAVYYCARQAWGYYALDIWGQGT ³ LVTVSSASTKGPSVF ⁴ PLAPSSKSTSGG TAALGCLYKDYFPEPVT ⁵ VSWSNGALTSGVHTT ⁶ PAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVN ⁷ NHKPSNTK VDKKVEPKSCDKTHTCTPPCPAPEAAGAPSVFL ⁸ PPKPKDITLMISRTPEVTCVVDVSHED ⁹ EVKFNWYVDG VEVHNAKTKPREEQYNSTYRVVSVLT ¹⁰ VLHQDWLNQKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL PPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNCPENNYK ¹¹ TPPVLDSDGSFFLYSKLTVDKSRWQQGN VFSCSYMIHEALHNHYTQKSLS ¹² CSPGK (SEQ ID NO: 23)
3F	EVQLVESGGGLVQPGGSLRLSCAASGFTESFEAMHWVRQAPGKGLEWVAKISPGGGSW ¹ TYSDTVTD ² DRFTF SLDTSKSTAYLQMNSLRAEDTAVYYCARQAWGYYALDIWGQGT ³ LVTVSSASTKGPSVF ⁴ PLAPSSKSTSGG TAALGCLYKDYFPEPVT ⁵ VSWSNGALTSGVHTT ⁶ PAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVN ⁷ NHKPSNTK

FIG. 22

	VDKKVEPKSCDKTHITCPPCPAPEAAGAPSVFLPPPKPKDILMISRTPEVTCVVVDVSHEDPEVKFNWYVDG VEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL PPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGN VFSCSVMBEALHNHYTQKSLSLSPGK (SEQ ID NO: 24)
3G	EVQLVESGGGLVQPGGSLRLSCAASGETTSPEAMHIVYRQAPGKGLEWYAKISPGGSWITYSDITYIDRFTF SLDTSKSTAYLQMNSLR AEDTAVYYCARQKQWGYALDIWQGGTLVTVSSASTKGPSVFPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHITFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKKVEPKSCDKTHITCPPCPAPEAAGAPSVFLPPPKPKDILMISRTPEVTCVVVDVSHEDPEVKFNWYVDG VEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL PPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGN VFSCSVMBEALHNHYTQKSLSLSPGK (SEQ ID NO: 25)
3H	EVQLVESGGGLVQPGGSLRLSCAASGETTSPEAISWVRQAPGKGLEWYAKISPGGSWITYSDITYIDRFTF LDTSKSTAYLQMNSLR AEDTAVYYCARQLWGYYALDYWQGGTLVTVSSASTKGPSVFPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHITFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKKVEPKSCDKTHITCPPCPAPEAAGAPSVFLPPPKPKDILMISRTPEVTCVVVDVSHEDPEVKFNWYVDG VEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL PPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGN VFSCSVMBEALHNHYTQKSLSLSPGK (SEQ ID NO: 26)
3I	EVQLVESGGGLVQPGGSLRLSCAASGETTSPEAWSWVRQAPGKGLEWYAKISPGGSWITYSDITYIDRFTF SLDTSKSTAYLQMNSLR AEDTAVYYCARQLWGYYALDYWQGGTLVTVSSASTKGPSVFPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHITFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKKVEPKSCDKTHITCPPCPAPEAAGAPSVFLPPPKPKDILMISRTPEVTCVVVDVSHEDPEVKFNWYVDG VEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL PPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGN VFSCSVMBEALHNHYTQKSLSLSPGK (SEQ ID NO: 27)

FIG. 22 (continued)

ID	Light chain
4A	DIQLTQSPSSLSASVGDRVTTTCSASISVSYLEWYQQKPGKAPKLLIYDDSSLASGVPSRFSGSGSGTDFTLTIT SSLQPEDFATYYCQQWSQYPYTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQ WKVDNALQSGNSQESVTEQDSKDSITYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 28)
4B	DIQLTQSPSSLSASVGDRVTTTCSASISVSYLEWYQQKPGKAPKLLIYDA9SLASGVPSRFSGSGSGTDFTLTIT SSLQPEDFATYYCQQWSQYPYTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQ WKVDNALQSGNSQESVTEQDSKDSITYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 29)
4C	DIQLTQSPSSLSASVGDRVTTTCSASISVSYLEWYQQKPGKAPKLLIYDDSNLASGVPSRFSGSGSGTDFTLTIT SSLQPEDFATYYCQQWSGYPTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQ WKVDNALQSGNSQESVTEQDSKDSITYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 30)

FIG. 23

ID	Heavy chain - Fab	Heavy chain - Fc
5A	EVQLVESGGGLVQPGGSLRLSCAASGFTSPFAM HWVRQAPGKGLFWYAKISPGGSWTYYSDTYTDR FTFSLDTSKSTAYLQMNSLRAEDTAVYYCARQA WGYYALDIWGQGTILVTVSSASTKGPSVFPLAPSS KSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSG VHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICN VNHKPSNTKVDKKVEPKSC (SEQ ID NO: 31)	DKTHITCPPCPAPEAAGAPSVFLFPPKPKDTLMISK TPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAK TKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKC KVSNAKALPAIEKTISKAKGQPREPQVYTLPPSREE MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFC SYMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 40)
5B	EVQLVESGGGLVQPGGSLRLSCAASGFTSPFAM HWVRQAPGKGLFWYAKISPGGSWTYYSDTYTDR FTFSLDTSKSTAYLQMNSLRAEDTAVYYCARQSW QYYALDIWGQGTILVTVSSASTKGPSVFPLAPSSKS TSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVH TFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVN HKPSNTKVDKKVEPKSC (SEQ ID NO: 32)	DKTHITCPPCPAPEAAGAPSVFLFPPKPKDTLMISK TPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAK TKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKC KVSNAKALPAIEKTISKAKGQPREPQVYTLPPSREE MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFC SYMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 41)
5C	EVQLVESGGGLVQPGGSLRLSCAASGFTSPFAM HWVRQAPGKGLFWYAKISPGGSWTYYSDTYTDR FTFSLDTSKSTAYLQMNSLRAEDTAVYYCARQG WGYYALDIWGQGTILVTVSSASTKGPSVFPLAPSS KSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSG VHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICN VNHKPSNTKVDKKVEPKSC (SEQ ID NO: 33)	DKTHITCPPCPAPEAAGAPSVFLFPPKPKDTLMISK TPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAK TKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKC KVSNAKALPAIEKTISKAKGQPREPQVYTLPPSREE MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFC SYMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 42)
5D	EVQLVESGGGLVQPGGSLRLSCAASGFTSPFAM HWVRQAPGKGLFWYAKISPGGSWTYYSDTYTDR FTFSLDTSKSTAYLQMNSLRAEDTAVYYCARQTW GYYALDIWGQGTILVTVSSASTKGPSVFPLAPSSKS TSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVH TFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVN HKPSNTKVDKKVEPKSC (SEQ ID NO: 34)	DKTHITCPPCPAPEAAGAPSVFLFPPKPKDTLMISK TPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAK TKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKC KVSNAKALPAIEKTISKAKGQPREPQVYTLPPSREE MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFC SYMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 43)
5E	EVQLVESGGGLVQPGGSLRLSCAASGFTSPFAM HWVRQAPGKGLFWYAKISPGGSWTYYSDTYTDR FTFSLDTSKSTAYLQMNSLRAEDTAVYYCARQV WGYYALDIWGQGTILVTVSSASTKGPSVFPLAPSS KSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSG VHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICN VNHKPSNTKVDKKVEPKSC (SEQ ID NO: 35)	DKTHITCPPCPAPEAAGAPSVFLFPPKPKDTLMISK TPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAK TKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKC KVSNAKALPAIEKTISKAKGQPREPQVYTLPPSREE MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFC SYMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 44)

FIG. 24

5F	EVQLVESGGGLVQPGGSLRLSCAASGFTISPFAM HWVRQAPGKGLFWYAKISPGGSWYYSDTYIDR PTISLDTSKSTAYLQMNSLRAEDTAVYYCARQK WGYYALDIHWGGGTLVTVSSASTKQPSVFPLAPSS KSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSG VHTFPAVLQSSGLYSLSSVTVTPSSSLGTQTYICN VNHKPSNTRVDKKVEPKSC (SEQ ID NO: 36)	DKTHITCPPCAPEAAAGAPSVFLFPKPKDILMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAK TKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKC KVSNAKALPAPIEKTISKAKGQPREPQVYTLPPSREE MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTTTPVLDSDGSHFLYSKLTVDKSRWQQGNVFSC SYMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 45)
5G	EVQLVESGGGLVQPGGSLRLSCAASGFTISPFAM HWVRQAPGKGLFWYAKISPGGSWYYSDTYIDR PTISLDTSKSTAYLQMNSLRAEDTAVYYCARQK WGYYALDIHWGGGTLVTVSSASTKQPSVFPLAPSS KSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSG VHTFPAVLQSSGLYSLSSVTVTPSSSLGTQTYICN VNHKPSNTRVDKKVEPKSC (SEQ ID NO: 37)	DKTHITCPPCAPEAAAGAPSVFLFPKPKDILMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAK TKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKC KVSNAKALPAPIEKTISKAKGQPREPQVYTLPPSREE MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTTTPVLDSDGSHFLYSKLTVDKSRWQQGNVFSC SYMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 46)
5H	EVQLVESGGGLVQPGGSLRLSCAASGFTISPFAM WVRQAPGKGLFWYAKISPGGSWYYSDTYIDR PTISLDTSKSTAYLQMNSLRAEDTAVYYCARQLW GYYALDIHWGGGTLVTVSSASTKQPSVFPLAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVTVTPSSSLGTQTYICNV NHHKPSNTRVDKKVEPKSC (SEQ ID NO: 38)	DKTHITCPPCAPEAAAGAPSVFLFPKPKDILMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAK TKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKC KVSNAKALPAPIEKTISKAKGQPREPQVYTLPPSREE MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTTTPVLDSDGSHFLYSKLTVDKSRWQQGNVFSC SYMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 47)
5I	EVQLVESGGGLVQPGGSLRLSCAASGFTISPEAW WVRQAPGKGLFWYAKISPGGSWYYSDTYIDRF PTISLDTSKSTAYLQMNSLRAEDTAVYYCARQLW GYYALDIHWGGGTLVTVSSASTKQPSVFPLAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVTVTPSSSLGTQTYICNV NHHKPSNTRVDKKVEPKSC (SEQ ID NO: 39)	DKTHITCPPCAPEAAAGAPSVFLFPKPKDILMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAK TKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKC KVSNAKALPAPIEKTISKAKGQPREPQVYTLPPSREE MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTTTPVLDSDGSHFLYSKLTVDKSRWQQGNVFSC SYMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 48)

FIG. 24 (continued)

ID	(SEQ ID NO.)	CDR1	(SEQ ID NO.)	CDR2	(SEQ ID NO.)	CDR3
3A / 5A	(49)	GFIFSPFAMH	50	AKISPGGSWTYYSDIVTD	51	ARQAWGYVALDI
3B / 5B	52	GFIFSPFAMH	53	VAKISPGGSWTYYSDIVTD	54	ARQSWGYVALDI
3C / 5C	55	GFIFSPFAMH	56	VAKISPGGSWTYYSDIVTD	57	ARQSWGYVALDI
3D / 5D	58	GFIFSPFAMH	59	VAKISPGGSWTYYSDIVTD	60	ARQTVGYVALDI
3E / 5E	61	GFIFSPFAMH	62	VAKISPGGSWTYYSDIVTD	63	ARQVWGYVALDI
3F / 5F	64	GFIFSPFAMH	65	VAKISPGGSWTYYSDIVTD	66	ARQQWGYVALDI
3G / 5G	67	GFIFSPFAMH	68	VAKISPGGSWTYYSDIVTD	69	ARQKWGYVALDI
3H / 5H	70	GFIFSPFAIS	71	VAKISPGGSWTYYSDIVTD	72	ARQLWGYVALDV
3I / 5I	73	GFIFSPFAWS	74	VAKISPGGSWTYYSDIVTD	75	ARQLWGYTALDV

FIG. 25A

ID	(SEQ ID NO.)	CDR1	(SEQ ID NO.)	CDR2	(SEQ ID NO.)	CDR3
4A	76	SASISVSYLY	77	LLYDDSNLAS	78	QQWNGYFYT
4B	79	SASISVSYLY	80	LLYDASSLAS	81	QQWNGYFYT
4C	82	SASISVSYLY	83	LLYDDSNLAS	84	QQWNGYFYT

FIG. 25B

(SEQ ID NO: 86)

(SEQ ID NO: 87)

(SEQ ID NO: 88)

ID	Sequence
6A	SDTGGPVPVNAFVNEPHEHEATGGKRLVTCCKVTPSPATVTLGGPPLDTLPQKQKRIHNSRGGQFDSNATYKSKL LTCEATVNGHLYKYNILTHPQDITIDVVLSPQKQKRLVNGKLVNCTARTFLPQGHDPVETYSRQKHL KKLVDKRLTQGHSDRPFLLTIDKPTKSDQKLYCAAGSLATKQKSTPLVTHKDKHTTCDPCAPAPA AGAPVPLPQQKDTLAGEPTVTVVYVSHDEPDKKXVYVYDVEHAKTSPRQDQYNTPTVVS VLTLLGQDLNKGKTYCKVGNALPAPKHTSKAGQGFQPVYTLPPRREKTHQSLTCLVKGPTP NDAVENENQGGQDQYNTPTVVLSDGSPFLYKLTVDKSRNQKQVFTCSVLSEALRSHYVTKQLSCSP GK
6B	SDTGGPVPVNAFVNEPHEHEATGGKRLVTCCKVTPSPATVTLGGPPLDTLPQKQKRIHNSRGGQFDSNATYKSKL LTCEATVNGHLYKYNILTHPQDITIDVVLSPQKQKRLVNGKLVNCTARTFLPQGHDPVETYSRQKHL KKLVDKRLTQGHSDRPFLLTIDKPTKSDQKLYCAAGSLATKQKSTPLVTHKDKHTTCDPCAPAPA AGAPVPLPQQKDTLAGEPTVTVVYVSHDEPDKKXVYVYDVEHAKTSPRQDQYNTPTVVS VLTLLGQDLNKGKTYCKVGNALPAPKHTSKAGQGFQPVYTLPPRREKTHQSLTCLVKGPTP NDAVENENQGGQDQYNTPTVVLSDGSPFLYKLTVDKSRNQKQVFTCSVLSEALRSHYVTKQLSCSP GK
6C	SDTGGPVPVNAFVNEPHEHEATGGKRLVTCCKVTPSPATVTLGGPPLDTLPQKQKRIHNSRGGQFDSNATYKSKL LTCEATVNGHLYKYNILTHPQDITIDVVLSPQKQKRLVNGKLVNCTARTFLPQGHDPVETYSRQKHL KKLVDKRLTQGHSDRPFLLTIDKPTKSDQKLYCAAGSLATKQKSTPLVTHKDKHTTCDPCAPAPA AGAPVPLPQQKDTLAGEPTVTVVYVSHDEPDKKXVYVYDVEHAKTSPRQDQYNTPTVVS VLTLLGQDLNKGKTYCKVGNALPAPKHTSKAGQGFQPVYTLPPRREKTHQSLTCLVKGPTP NDAVENENQGGQDQYNTPTVVLSDGSPFLYKLTVDKSRNQKQVFTCSVLSEALRSHYVTKQLSCSP GK
6D	SDTGGPVPVNAFVNEPHEHEATGGKRLVTCCKVTPSPATVTLGGPPLDTLPQKQKRIHNSRGGQFDSNATYKSKL LTCEATVNGHLYKYNILTHPQDITIDVVLSPQKQKRLVNGKLVNCTARTFLPQGHDPVETYSRQKHL KKLVDKRLTQGHSDRPFLLTIDKPTKSDQKLYCAAGSLATKQKSTPLVTHKDKHTTCDPCAPAPA AGAPVPLPQQKDTLAGEPTVTVVYVSHDEPDKKXVYVYDVEHAKTSPRQDQYNTPTVVS VLTLLGQDLNKGKTYCKVGNALPAPKHTSKAGQGFQPVYTLPPRREKTHQSLTCLVKGPTP NDAVENENQGGQDQYNTPTVVLSDGSPFLYKLTVDKSRNQKQVFTCSVLSEALRSHYVTKQLSCSP GK

FIG. 26

Light chain sequence
DQQLTQNPSSLASVGDHRYTTCSSASISLLEWYQQKPKAPKLLDDSSSLAKCVPSRPSGSGGTDTLTLSLQPEDFAVYTCQDDESGCLPDTFGQGTAKVEIKRTVAAPSVEPPPS
DEQLKSGTASVAVCLLNFPYREAKVQWKVDNALQSGNSQESVTEQDSKDSYSTSYSLSTLTLSKADAEKHKVYACEVTHQGLSSPVTKSFNRCHC (SEQ ID NO: 169)

VL
CDR (Kabat numbering)

Heavy chain sequence with notations
SDTCRPFVEMYSSEPMHMMTEGRHELVPCRVTSNPNTVTLKKPPI DTLDDGCKRWVDSKKGFHSNATYKEHGLTICEATVNGHLYKTNVLTTRQINTIIDNVLSFSGHSELSTV
GEKLVLNCTARTELNVGHFNWETPSSKHHQHKLVNRDLKTQSGSEMKRFLSTLTIDGVTIRSDQGLYTC AASSGLMIRKNSITFVVRHEKGGSGGGSGGSFVQLVESG
GGLVQPPGSLRLSCAASGFTFSELAHWRVQRQAPCGAGLEWPAKESGGEWLEKDLIDRFTSLDINASTATLQMASLRAEDTAVTYCARQAHGGLLALRWGGGLVYSSASTK
GPSVHPLAPSSKSTSGGTAAALGCLVKDYTPPEPTVSWNSGALTSGVHTTPAVLQSSGLYSLSVVTVPSSSLGTQTYICNVNHRPSNTKVVDKKVEPKSCDKTHITCPCPAP
EAAAGAPSVFLPPPKKIDTLMSKRTPEVTCVAVDVSHEDPEVKENWYVDGVEVHNARTKPREEQYNSTYRVVSVLTVLDHODWLNQKEYKCKVSNKALPAPIEKTHKAK
GQPREPQVYTLPPSREEMTKNQVSLTCLVRGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFPLYSKLTVDKSRWQQGNVSTCSVMHEALHINHYTQKSLSLSPGR
(SEQ ID NO: 170)

VEGFR
Linker
VH
CDR (Kabat numbering)

FIG. 27

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Figure 28

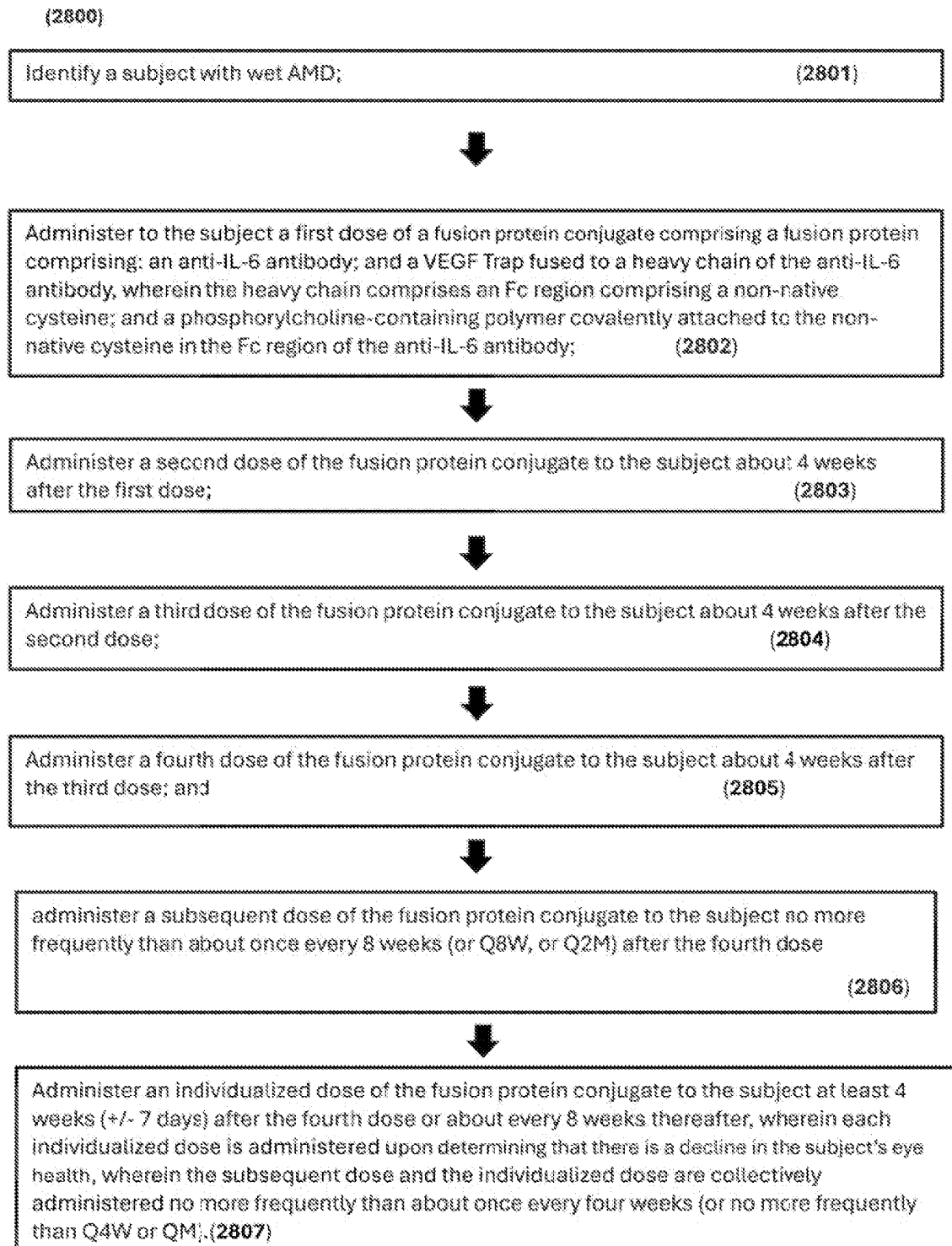
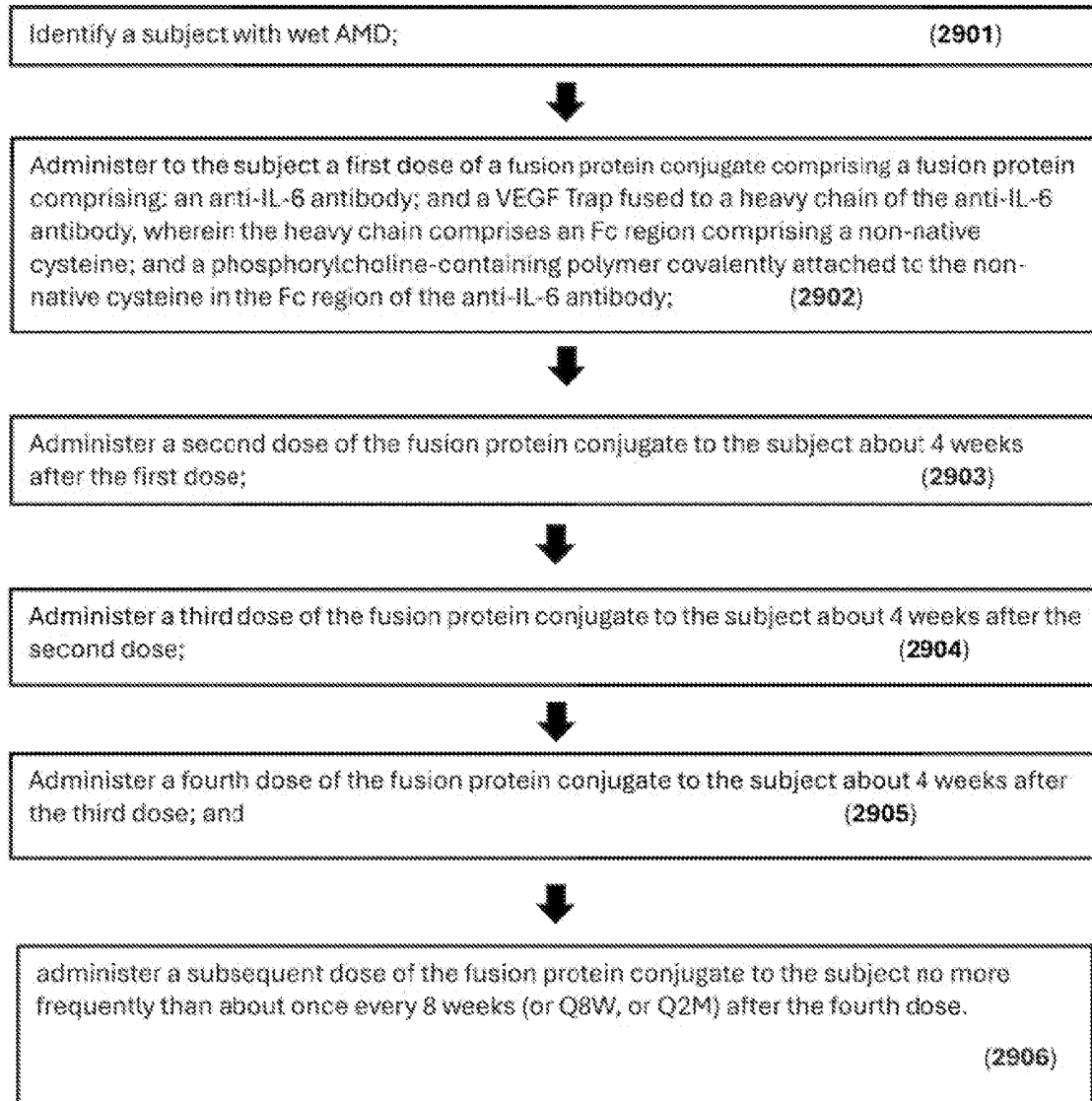


Figure 29

(2900)



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Figure 30

(3000)

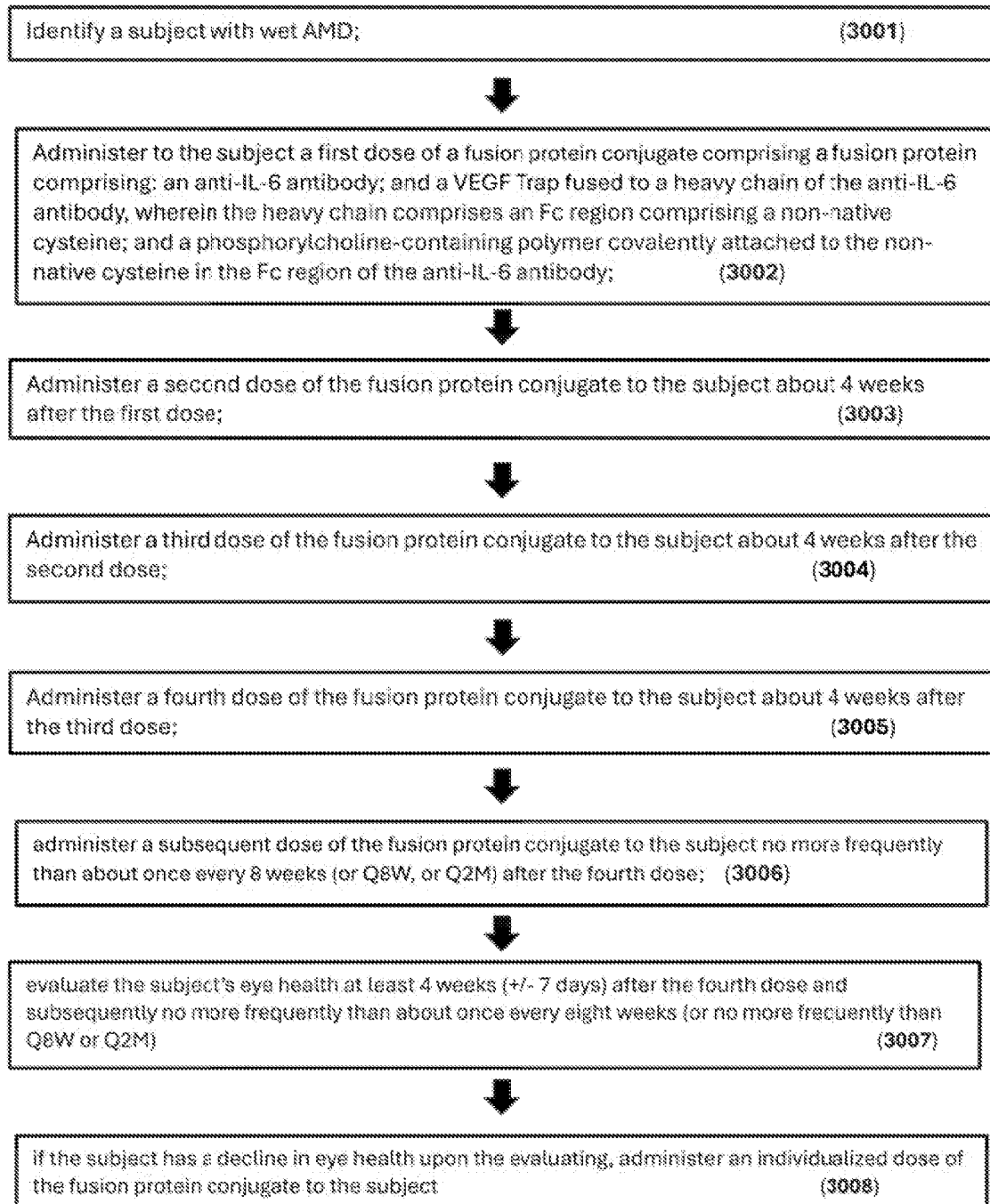
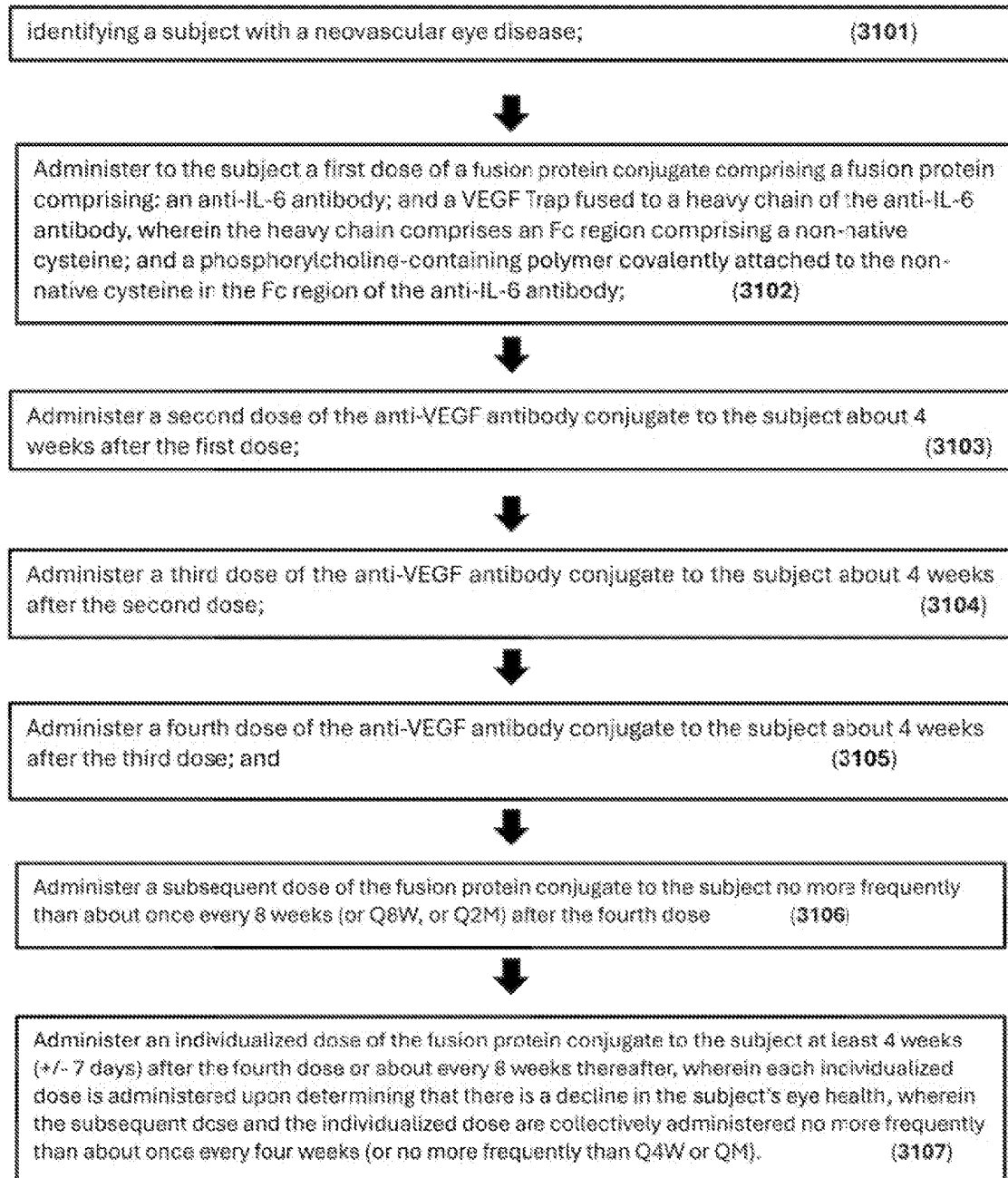


Figure 31

(3100)



(3200)

Administer to a subject in need thereof 4 loading doses of a fusion protein conjugate comprising a fusion protein comprising: an anti-IL-6 antibody; and a VEGF Trap fused to a heavy chain of the anti-IL-6 antibody, wherein the heavy chain comprises an Fc region comprising a non-native cysteine; and a phosphorylcholine-containing polymer covalently attached to the non-native cysteine in the Fc region of the anti-IL-6 antibody; (3201)



Administer a subsequent dose of the fusion protein conjugate to the subject no more frequently than about once every 8 weeks (or Q8W, or Q2M) after a last loading dose; (3202)



Determine, at least 4 weeks (+/- 7 days) after a last loading dose and/or about every 8 weeks thereafter, the presence of intraretinal fluid (IRF) and/or subretinal fluid (SRF) in an eye of the subject, and/or if macular hemorrhage due to wAMD activity has clinically worsened; and (3203)



If there is IRF or SRF in the eye, or the subject has clinically worsened macular hemorrhage due to wAMD activity, administer a maintenance dose fusion protein conjugate. (3204)

FIG. 32

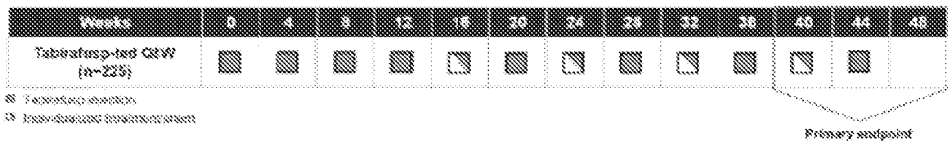


FIG. 33

KSI-101 is a first-in-class bispecific protein for the powerful treatment of macular edema secondary to inflammation (“MESI”)

- KSI-101 is a bispecific protein designed to directly target both IL-6 mediated inflammation and edema, and VEGF-mediated vascular permeability

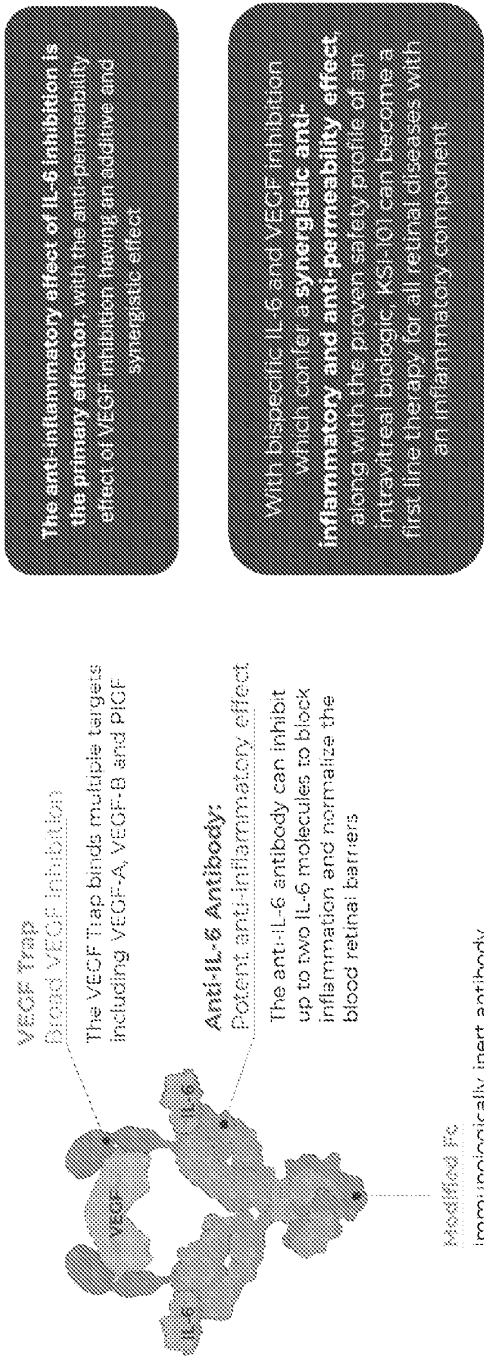
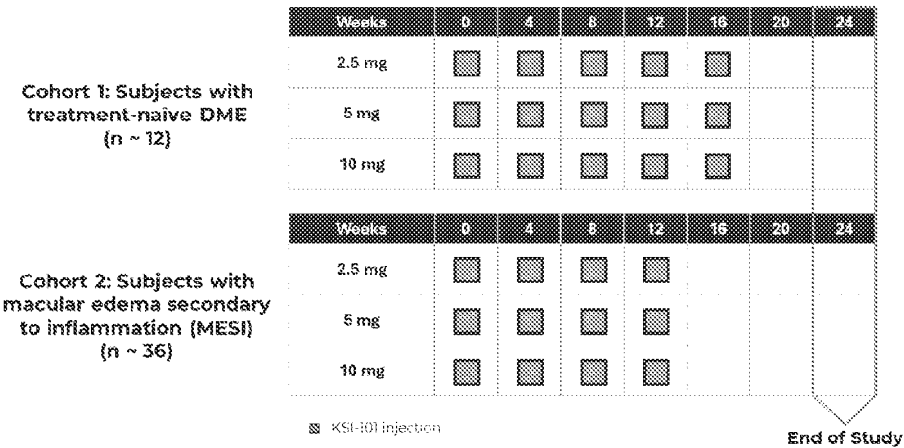
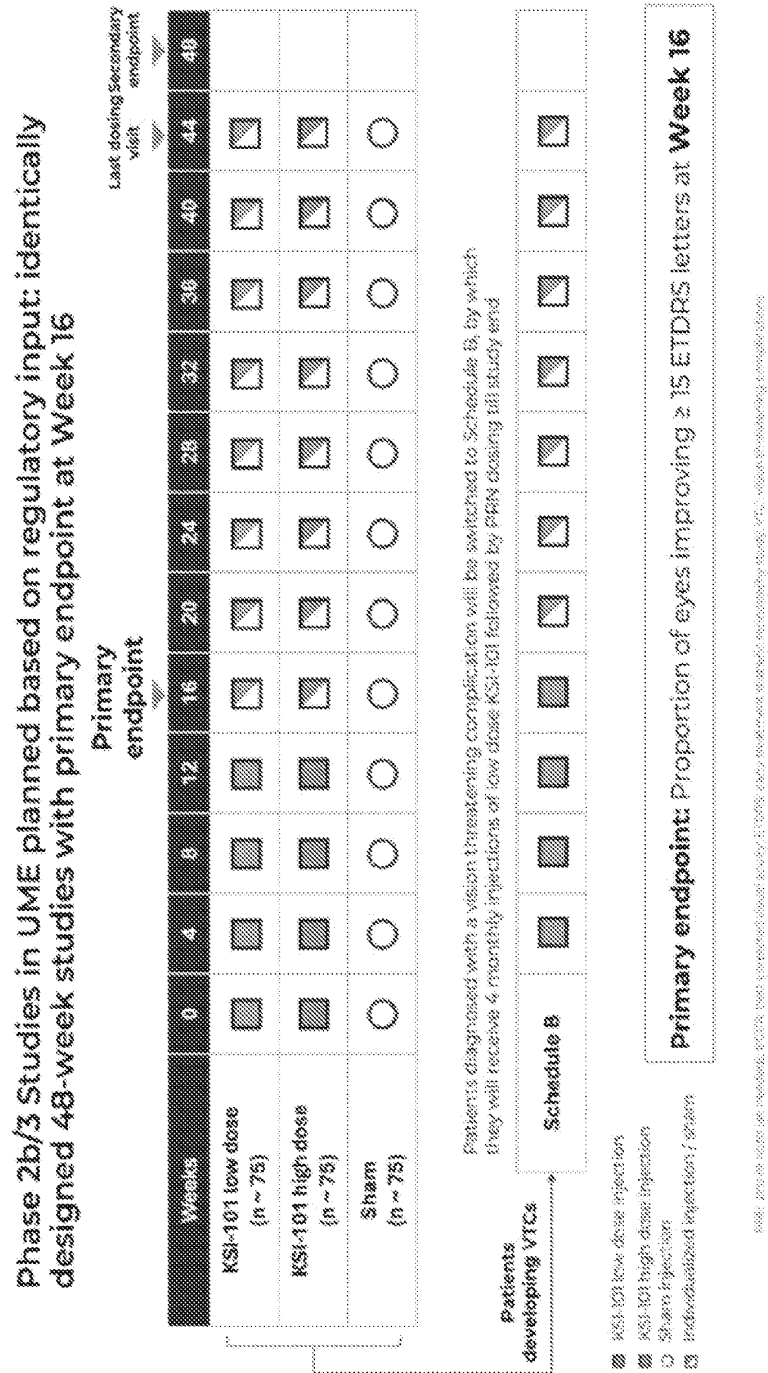


FIG. 34



A low and high dose of KSI-101 will be selected to progress into dual Phase 2b/3 pivotal studies in MESI

FIG. 35



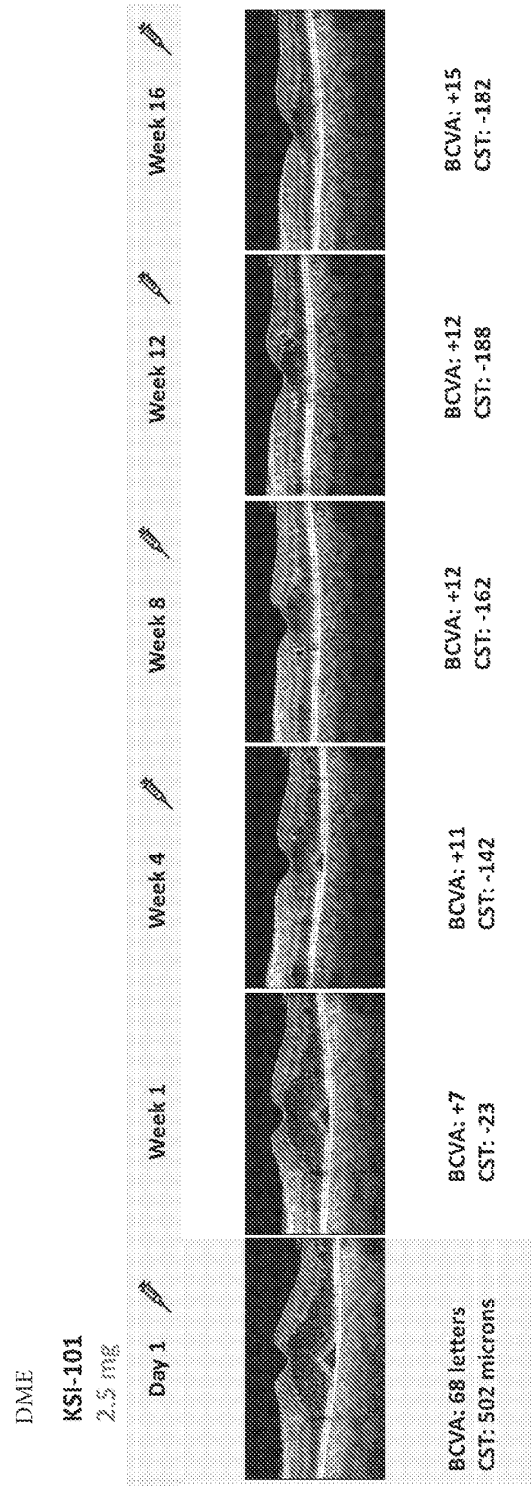


FIG. 37A

DME
KSI-101
5 mg

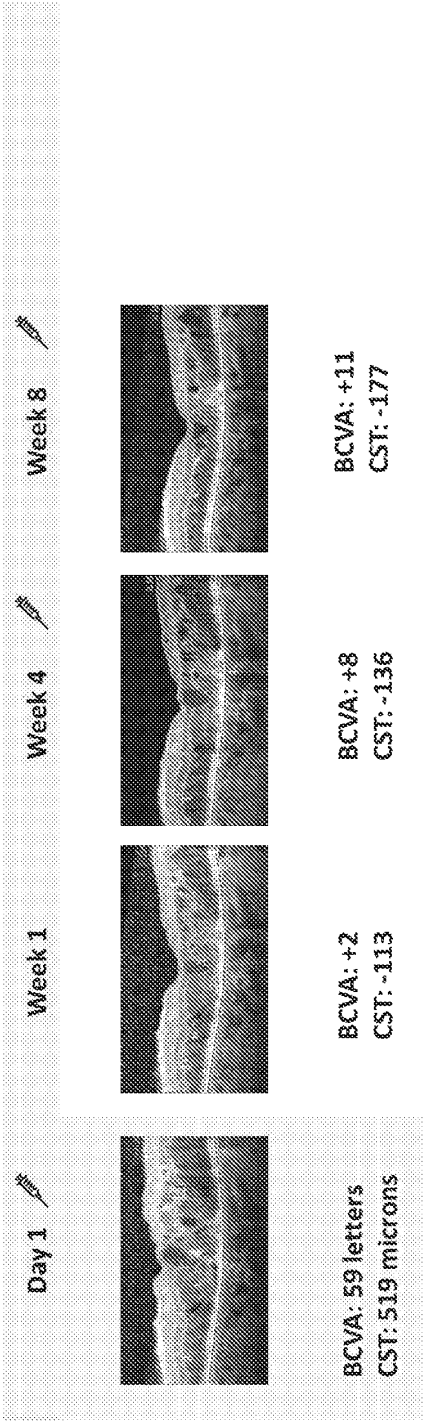


FIG. 37B

DME

KSI-101

10 mg

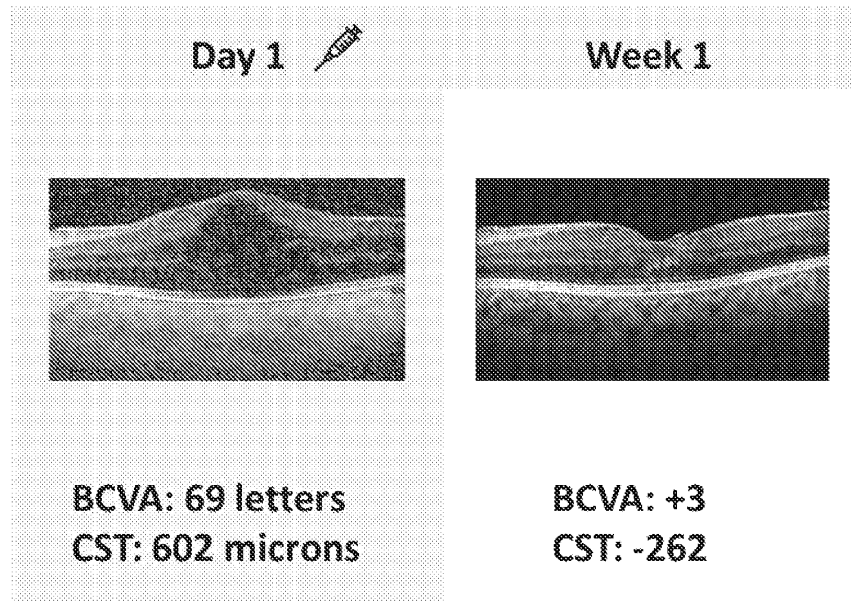


FIG. 37C

Macular edema secondary to inflammation

KSI-101
2.5 mg

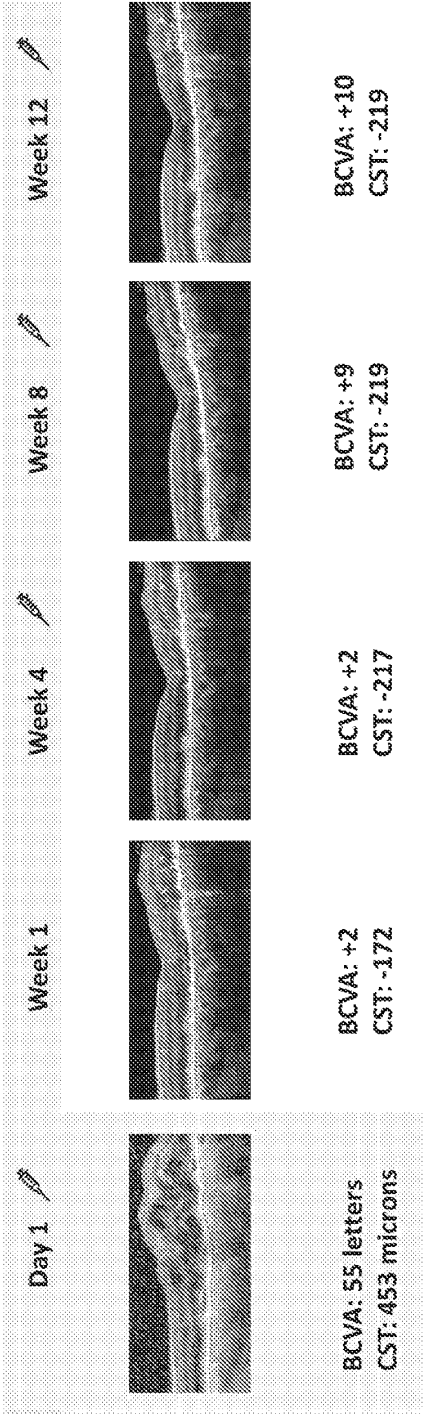


FIG. 38A

Macular edema secondary to inflammation

KSI-101
5 mg

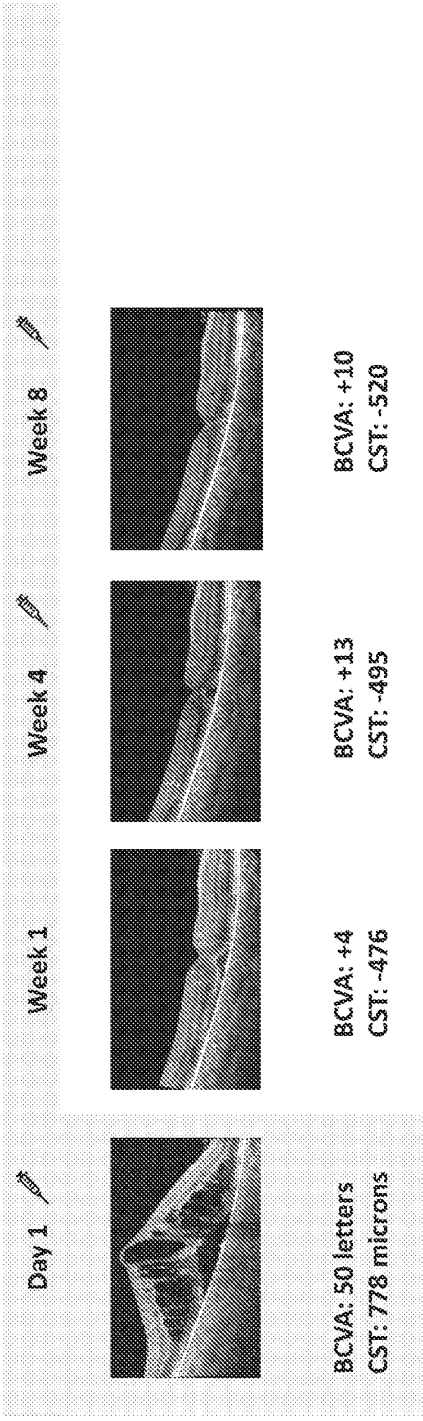


FIG. 38B

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Macular edema secondary to inflammation

KSI-101

10 mg

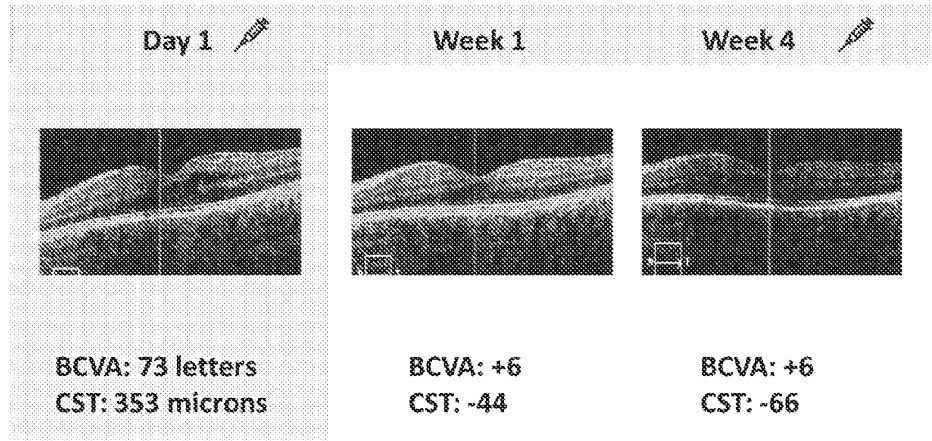


FIG. 38C